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DANIAE, FENNIAE, NORVEGIAE, ET SUECIAE

VOL. 39 FEBRUARY 1953 FASC. 2

HEPATIC VENOGRAPHY IN MAN

by

G. Tori

In recent years much attention has been paid to the problem of rendering the vessels of the liver radiologically visible.

The visualization of the hepatic artery and its interparenchymal branches may be obtained by abdominal aortography. However, the degree of opacity is always relatively poor, since the contrast medium usually outlines the abdominal aorta rather than its branches (with the exception of the renal arteries which are often well shown).

The venous afferent system of the liver may be demonstrated in living man by means of venography during laparatomy. The technique consists in the injection of a contrast medium into one of the branches or the main trunk of the portal vein through direct puncture or after the insertion of a fine catheter of polythene (MOORE). BLAKEMORE, LEGER and co-workers have used this technique to study the site of extra-hepatic portal obstruction in Banti's disease, and SANTY and MARION have utilized it to investigate the morphology of the portal vein with a view to the possibility of establishing an anastomosis between the portal and inferior vena cava systems for the cure of portal hypertension.

ABEATICI and CAMPI have obtained the same results without resorting to laparotomy by injecting the portal system through transparietal puncture of the spleen. Experiments carried out in dogs have demonstrated that the spleen under the stimulus of injection vigorously contracts, expelling the contrast medium and rendering the intra- and extrahepatic systems radio-opaque. In man intrasplenic transparietal portography has already been applied in normal and pathologic cases by LEGER, BOULVIN, SOTGIU and co-workers.

The hepatic efferent system has not apparently been studied in man. Contrast filling of the main trunks of the hepatic veins, however, may

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From the Roentgen Institute (Director: Prof. G. G. PALMIERI) of Bologna University, Bologna. Italy.

be obtained during angiocardiographies in children and selective angiocardiographies in adults.

RAPPAPORT has recently described a method of rendering the hepatic veins in the dog visible by catheterization. The technique consists in introducing a special catheter through the saphenous vein and advancing it into the inferior vena cava as far as the opening of the hepatic veins. The catheter used is fitted with an internal metallic guide which permits exploration of the right or left hepatic veins at will. Once the extremity of the catheter is situated in the vein which it is desired to visualize, the metallic guide is removed and 20 cc of Diodrast 70 % are injected. According to the author it is thus possible to obtain sufficient opacity of the major hepatic veins and their finer ramifications.

The technique which the author has used in living human subjects is based on the catheterization of the hepatic veins. The catheter is introduced in the right auricle but instead of the tip being pushed forwards towards the tricuspid valve into the right ventricle, it is, with delicate movements of axial torsion directed posteriorly and at the same time carefully rotated in contact with the posterior wall of the right auricle. As the catheter is advanced still further the inferior vena cava is reached without difficulty. Sometimes the introduction of the catheter into the inferior vena cava takes place immediately; at all events catheterization is effected in every case. The tip of the catheter is directed along the inferior vena cava in stages in order to determine precisely the length of the vessel. It is then slowly retracted and rotated to the right or the left until the openings of the hepatic veins, situated approximately 2—3 cm below the diaphragm, are presumed to have been reached. Again directed forwards the tip of the catheter is introduced into the hepatic vein selected.

The introduction of the catheter into the considerably larger right branches is relatively easy, enabling the peripheral regions to be reached. The catheter, even when of fairly fine narrow calibre (we generally use a Cournand 9—12), enters the left branches less readily, partly because of the narrower lumen of the vessels and partly because these divide immediately so that the catheter is impeded. When it has been confirmed by fluoroscopy that the catheter has been introduced into the right or the left superior group of veins, 20—25 cc of the contrast medium at the rate of 4—5 cc per second are injected.

Two or three radiograms may be obtained at intervals of 1 or 2 seconds while the patient is in apnea, so that the flow of the contrast medium may be recorded before it disappears from the arborizations of the catheterized and adjacent vessels and returns to the right auricle. The radiograms are made with the subject in the supine position. In

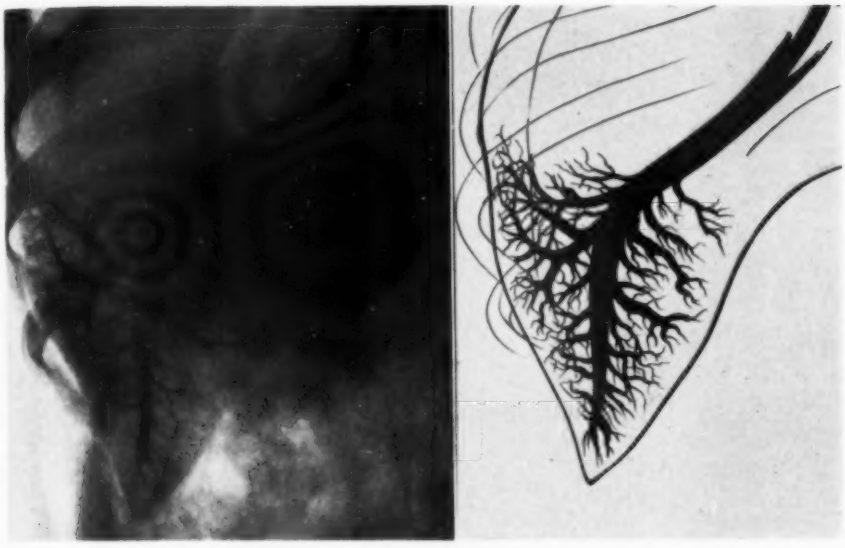

Fig. 1. Injection of the right hepatic veins after catheterization. The main trunk and most of the smaller branches are clearly defined.

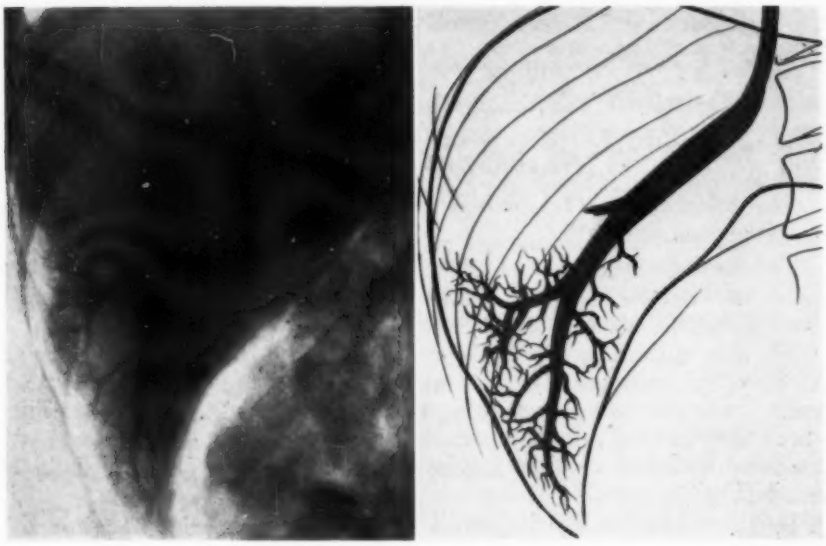

Fig. 2. Visualization of the main trunk of the right hepatic veins and the fine peripheric branches.

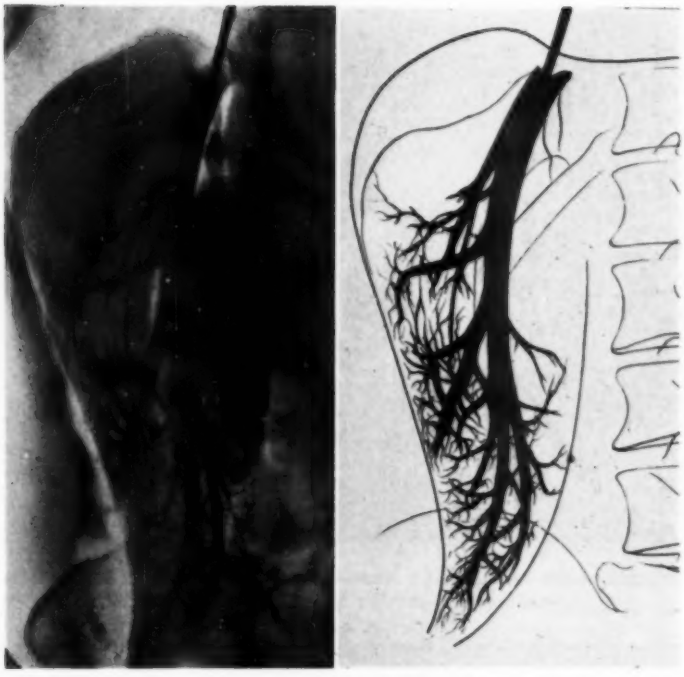

Fig. 3. Almost complete injection of the right hepatic venous system.

order to demonstrate the liver to the best advantage preliminary moderate quantities of oxygen are introduced into the retroperitoneal space.

The tolerance to the method by the ten patients in whom it was exhibited was excellent.

The radiograms obtained demonstrated a satisfactory visualization of the right hepatic veins as far as their terminal branches (Figs. 1—4). The left hepatic veins were generally more difficult to show.

We also studied two pathologic cases. In the first, with an enlarged and knobbly liver and a clinical suggestion of malignancy, the contrast medium was introduced into the main right trunk; the contrast filling practically terminated at a certain point and only a few secondary branches displaced at right angles presumably by a growth, could be traced (Fig. 5).

In the second case, diagnosed as myeloid leukemia, the injection only of the left superior group was carried out. The configuration of the

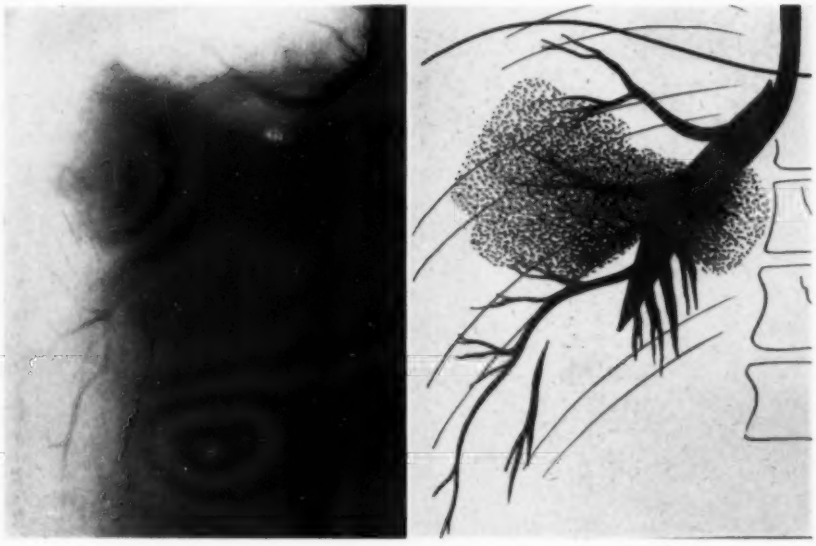

Fig. 4. Injection of the right superior group of hepatic veins. As the more or less large main trunks are visualized, several opacities due to contrast medium collecting in the intralobular capillaries, appear.

hepatic vessels of the left lobe was obviously different from the normal (Fig. 6).

During the contrast filling of the hepatic veins, a relatively common occurrence is the appearance of adjacent, sometimes extensive opaque areas. In order that the genesis of these areas may be explained, certain anatomic factors of the hepatic efferent venous system must be briefly detailed.

The blood carried to the liver by the portal vein and the hepatic artery, is collected from the sinusoids by the intralobular veins; these unite to form the sublobular veins which in turn open into the hepatic veins. The latter enter the inferior vena cava as it lies in the groove on the posterior surface of the liver.

The hepatic veins are arranged in two groups: superior and inferior. The superior group includes two large veins which empty into the inferior vena cava immediately below the vena-caval opening of the diaphragm; the right vein is formed by two large canals from the right lobe of the liver and which unite 1—2 cm before the anastomosis. The left is made up of two or three large canals which collect the blood from the left and in part from the right lobe (Fig. 7).

Fig. 5. Catheterization and injection of the right lobe venous system in a suspected case of liver neoplasm. The contrast medium is held up after 8 cm of the main trunk have been filled: only a few secondary branches standing out at almost right angles may be observed.

The inferior group, on the other hand, consists of a variable number of small vessels (which open by means of minute orifices lying inferiorly to the two larger veins) which come from the right lobe and from the lobe of Spigelius. Within the liver the hepatic veins are distinguished from the portal veins by (1) their anteroposterior direction, (2) their adherence to the hepatic tissue so that on section they remain widely open and by (3) the large number of small confluent vessels which open into them.

On examining the lumen of the larger hepatic veins, even in the proximity of their openings into the inferior vena cava, the presence of numerous orifices of extremely variable calibre (from 1 mm down to microscopic sizes) may be observed. These constitute the openings of a large number of more or less minute veins of short intraparenchymal course.

The characteristic structure of the efferent venous tree and its connections with the hepatic parenchyma offers an explanation of the genesis of the shadows noted. If the catheter more or less completely obliterates the lumen of the vessel or the tip is pressed against the wall or lies at level of a perpendicular branch, the injection of the contrast

Fig. 6. Injection of the left superior group of veins in a case of myeloid leukemia. An opaque patch is seen in the region of the middle-sized trunks, the finer branches probably showing an abnormal distribution.

medium causes an increase in local pressure (it will be recalled that the injection is performed against the blood stream). As a consequence, the contrast medium in addition to penetrating canals of considerable calibre which branch peripherally, also reaches the small veins which open at a level of the site of injection and diffuses successively into the intralobular veins and the sinusoids.

That this is the course of events, is confirmed by histologic sections of injected zones (in which blotchy patches adjacent to the venous configuration had appeared in roentgenograms previously obtained).

On the other hand the fact that satisfactory injection is obtained without the appearance of blotches when the catheter lies in the lumen of the vein without occluding it, may constitute further proof. In other words, in-

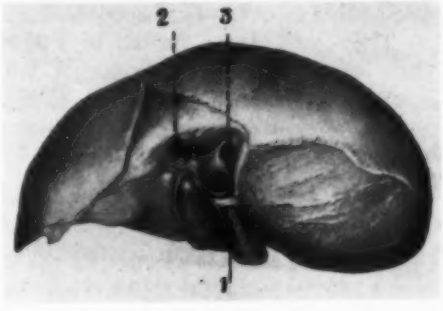

Fig. 7. Posterior border of liver. 1) inferior vena cava; 2) outlet of the left superior group of hepatic veins; 3) outlet of the right superior group of hepatic veins.

creased local pressure, determined by anatomic and functional factors and by circumstances intimately related with the position of the catheter, plays a pre-eminent rôle in the causation of the blotches.

Originally, since these blotchy images had been seen in the course of hepatic venography in subjects with increased intrahepatic pressure, it was believed that they were of pathologic significance. Their appearance, however, in obviously normal cases and in one in which a primary injection had produced good visualization without their appearance, strongly suggested that a collateral phenomenon related to the technique was involved; this, in some cases, unfortunately, cannot be obviated. The appearances tend to disappear rapidly, in fact are not evident roentgenographically 4—5 seconds after the completion of the injection.

Conclusions

The method described permits a satisfactory study of the hepatic venous outflow. The majority of cases, with the exception of two in which it was applied, were normal; in one the investigation helped to confirm the clinical diagnosis of hepatic neoplasm. For the time being, no definite opinion on the practical possibilities of the proposed method can be expressed. Its application in a larger number of pathologic cases may eventually demonstrate its usefulness.

The anatomy and functions of the intra-hepatic circulation and the liver parenchyma are intimately connected and when changes occur in the body of the organ, the hepatic veins of necessity must undergo profound modification. Theoretically therefore, the radiologic study of hepatic venous outflow, although to a lesser extent than portography, will contribute to the diagnosis of all those conditions of liver accompanied by circulatory disorders.

The method, as far as is known, has no contra-indications other than those normally associated with this type of contrast medium; it may be employed therefore, should portography prove unsatisfactory owing to raised intra-hepatic pressure in the portal veins or to extra-hepatic obstruction.

SUMMARY

The author describes a method for the study of the hepatic venous outflow in man. After a presentation of the results obtained in normal and in pathologic cases an interpretation of the blotchy patches which appear adjacent to the injected hepatic veins, is given.

The writer does not feel justified in expressing any opinion as yet on the practical possibilities of the method. Only its application in a larger number of pathologic cases will indicate its value.

ZUSAMMENFASSUNG

Der Verf. beschreibt eine Methode zum Studium des venösen Blutverlaufes in der Leber des Menschen. Nach einer Schilderung der Resultate in normalen und pathologischen Fällen wird eine Erklärung über die fleckigen Trübungen, welche neben den injizierten Lebervenen auftreten, gegeben.

Der Verf. fühlt sich noch nicht dazu berechtigt, etwas über die praktischen Möglichkeiten dieser Methode auszusagen. Nur ihre Anwendung in einer grossen Anzahl von pathologischen Fällen kann den Wert der Methode aufzeigen.

RÉSUMÉ

L'auteur décrit une méthode d'étude de la circulation veineuse de retour du foie chez l'homme. Après avoir présenté les résultats obtenus dans des cas normaux et pathologiques, il donne une interprétation des opacités en taches qui apparaissent au voisinage des veines hépatiques injectées. L'auteur ne se sent pas autorisé à exprimer actuellement une opinion sur les possibilités pratiques de cette méthode. Seule une application à un plus grand nombre de cas pathologiques indiquera sa valeur.

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ON THE VISUALIZATION OF ULCERATIVE PROCESSES USING HYDROGEN PEROXIDE IN THE CONTRAST MEDIUM

A preliminary report

by

Paavo Klami

In the diagnosis of pathologic ulcerative processes of the internal organs, the discharge of blood and pus from the diseased tissue into the excretions has for a long time been recognized as a significant sign. The appearance of red and white cells in the urine is one of the chief indications of renal tuberculosis. This factor forms a means of establishing cancer of the alimentary canal by the detection of occult haemorrhage. The laboratory tests used for this purpose are, in general, based on the property of haemoglobin to break down hydrogen peroxide, the oxygen thus liberated, together with other substances, producing a stain reaction. Further, the leucocytes also are able to reduce hydrogen peroxide into its elements, a fact which causes, for example, a marked formation of foam when cleansing an ulcer bathed in pus. It occurred to the author when considering the difficulty of the early diagnosis of carcinoma, that hydrogen peroxide might perhaps render the localization of ulceration in certain endoscopies and roentgen examinations more easy.

In recent years the writer has experimented on these lines in roentgen examinations of cases in which carcinoma of the oesophagus or stomach was suspected, and particularly when there was a question of the differential diagnosis between cicatricial and ulcerative changes. In this paper some of the more typical cases of this type together with some which

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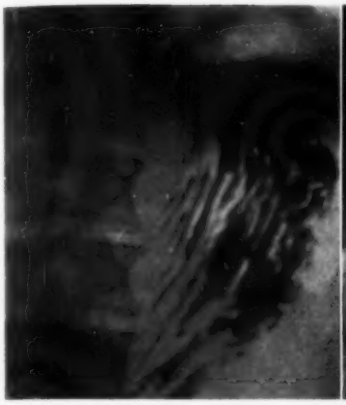


Fig. 1. Case 1. Normal stomach. No foam formation in contrast medium containing H_2O_2.

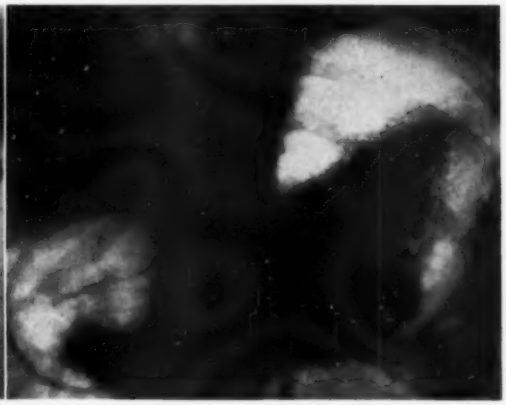
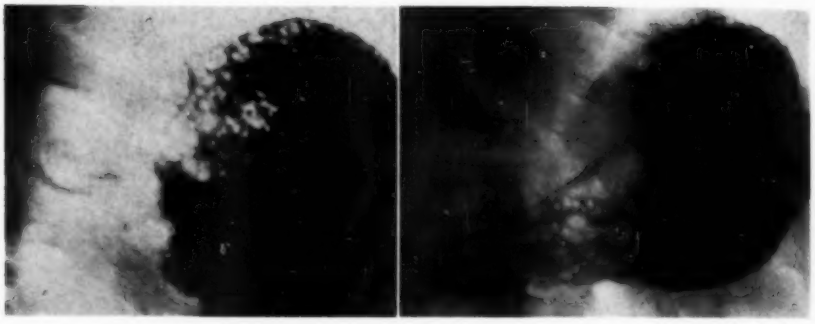


Fig. 2. Case 2. Haemorrhagic gastritis (patient prone; air-insufflation). Foam formation over the periphery of the contrast medium containing H_2O_2.

were normal are presented. An ordinary barium sulphate preparation (Barycon or Astrabaryt) mixed with 3 % hydrogen peroxide in water was used as a contrast medium in the examinations. When this medium is employed a formation of foam and a bubbly filling defect is to be expected in the region where the ulceration process is situated in the alimentary canal provided that there is no further blood or pus in the area — that is to say, provided any blood or pus is removed by lavage just before the examination. In investigations carried out with 20 Ewald test meals (both achylic and hyperacidic) it was proved that the gastric contents did not, from a practical point of view, cause any foam formation in the hydrogen peroxide, with two exceptions, in both of which specimens blood was found. Subsequent to this no foam formation was visible in films of the stomach of several patients in whom neither ulceration nor neoplasm were detected on roentgen examination.

Case 1. L. B., a machinist, aged 23. The clinical examination suggested probable colitis. Roentgen examination of the stomach, March 1948: no ulcer, neoplasm or any definite signs of gastritis found. No foam formation in the contrast medium, containing H_2O_2, visible. After a control period lasting over 3 years, no gastric symptoms (Fig. 1).

On the contrary marked foam formation appeared in several stomachs in which a clinical diagnosis of gastritis hemorrhagica had been made.



a. b.

Fig. 3, Case 3. Carcinoma cardiae. a. (Patient prone). Foam formation commencing around the cardiac region. b. (Patient supine; after 2 min.) Foam formation spreads over entire stomach. Large filling defect visible around cardia.

Case 2. H. K., a charwoman, aged 41. Treated for 5 years for achylic gastritis. Ewald test meal: 50 cc of well digested stomach contents containing a slight amount of blood, HCl—TA 4. Roentgen examination with contrast medium containing H_2O_2, plus air insufflation, March 1948: no signs of ulcer or neoplasm; marked foam formation over entire stomach wall. After a control period of over 4 years, practically symptomless. Apparently a case of hemorrhagic gastritis (Fig. 2).

In examinations of the stomach in which carcinoma had been previously established roentgenologically, foam formation occurred when a contrast medium containing hydrogen peroxide was employed.

Case 3. I. B., a fisherman's wife, aged 73 years. For 5 months, loss of weight; for 3 months, difficulty in swallowing, pain in the epigastrium and vomiting. Examination of stomach: filling defect at cardia, due apparently to large tumour. Marked foam formation in the contrast medium containing H_2O_2 commencing in the cardiac region. Patient discharged from hospital as inoperable; died at home shortly afterwards (Fig. 3 a and b).

There was one exception of no foam formation in an obvious gastric carcinoma.

Case 4. H. M., a tailor, aged 65. For 4 months, indefinite pain in the epigastrium. Slight resistance in epigastrium on palpation. Roentgen examination of stomach, Aug. 1948: almost over the entire stomach area, smooth-edged filling defects typical of a growth. No foam formation in the contrast medium containing H_2O_2. Laparotomia explorativa: carcinoma ventriculi inop. One lymph node was removed for examination. Pathologic findings: adeno-carcinoma ventriculi. As the stomach was not opened in the exploratory laparotomy it remained undecided whether the tumour in question was ulcerated or not. The smooth edges of the defects visible in the roentgen examination in addition to the absence of foam formation suggest the latter.

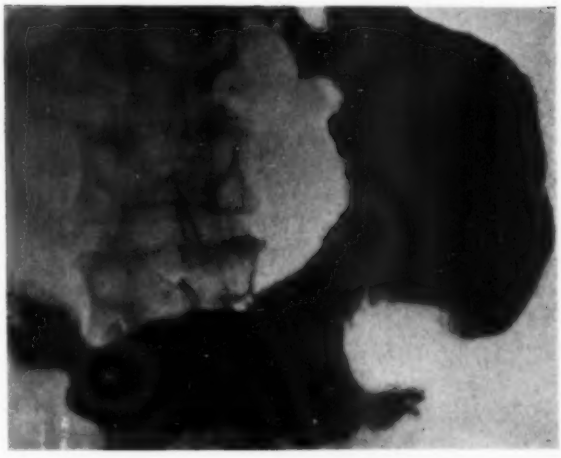


Fig. 4. Case 4. Carcinoma infiltrating almost entire stomach. No noteworthy foam formation.

As foam formation takes place both in cases of gastritis and ulcerative carcinomas, it seems that the examination in this form has only a limited significance in the diagnosis of gastric carcinomas *i. e.* when the result is negative. On the other hand, considerably better results have been obtained in the examination of narrow passages such as the oesophagus.

Case 5. O. P., a lawyer, aged 40. No symptoms suggesting oesophagus disease. Roentgen examination of the oesophagus was performed using a contrast medium containing H_2O_2 Oct. 1950: the same kind of roentgen appearances were obtained of the oesophagus as of a normal oesophagus when ordinary contrast medium is used. No foam formation. The patient was still symptomless in Aug. 1952 (Fig. 5).

Case 6. K. S., a female post office clerk, aged 36, was examined in April 1951 for occasional difficulty in swallowing. The clinical examination was unproductive and the roentgen findings negative; there was no foam formation in the contrast medium containing H_2O_2. The symptoms grew no worse during a control period lasting over a year (Fig. 6).

Case 7. S. L., a housewife, aged 45. Oesophageal corrosion (NaOH) in youth. The stricture which followed was treated by dilatation over a period of years. At the end of 1950 the stricture narrowed in spite of the passage of probes (only a No. 22 probe could be passed) and she complained of pain in the chest. Since malignant degeneration was suspected, roentgen examination was carried out in Nov. 1950, with a contrast medium containing H_2O_2 and revealed a funnel-shaped, smoothedged stricture at the level of the arcus aortae. No foam formation was visible in the contrast medium nor the usual signs of malignant changes. Probes were passed continuously,

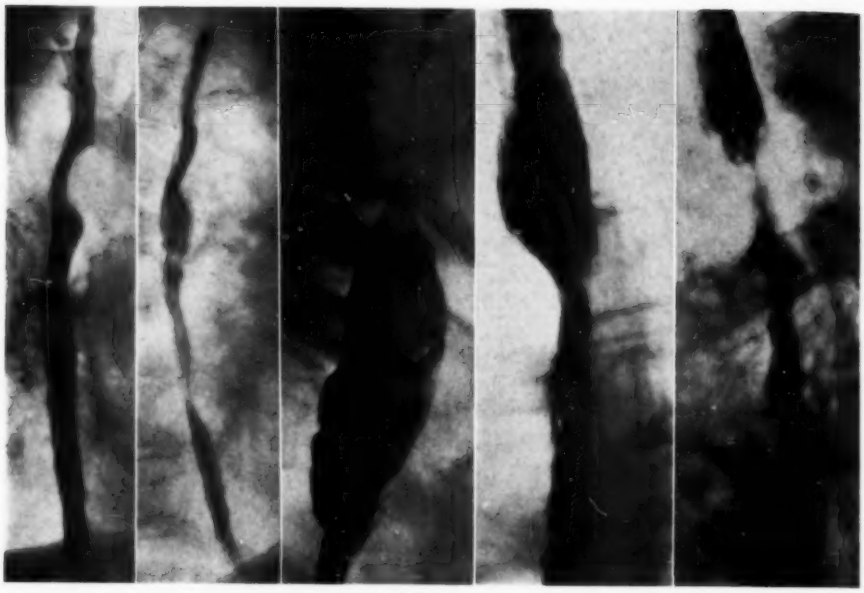


Fig. 5. Fig. 6. Fig. 7. Fig. 8 a. 8 b.

Fig. 5, Case 5, and Fig. 6, Case 6. Normal oesophagus. No foam formation in contrast medium containing H_2O_2.

Fig. 7, Case 7. Stricture caused by NaOH corrosion of oesophagus; benign. No foam formation in contrast medium containing H_2O_2.

Fig. 8, Case 8. Carcinoma oesophagi a. Ordinary contrast medium. b. Foam formation in contrast medium containing H_2O_2 displaces medium from affected area.

the last time in June 1952. The size of the probe alternated between a No. 26 and a No. 29. Apparently the case was not, during the examination, one of malignancy (Fig. 7).

In the normal oesophagus (Cases 5 and 6) and in some cases of stricture examined (Case 7) foam formation was never established. On the other hand, in the case of ulcerating processes definite foam formation takes place some tens of seconds after the commencement of the examination and pushes the contrast medium away from the affected region in both directions (Cases 8, 9 and 10).

Case 8. J. T., a carpenter, aged 54. For two years, smarting in the chest; for one year food had gone down with more difficulty than usual. Roentgen examination of oesophagus, Feb. 1948: carcinoma oesophagi. Marked foam formation, which displaced the contrast medium from the tumour area, occurred with contrast medium containing H_2O_2. Died August 1948 (Figs. 8 a and 8 b).

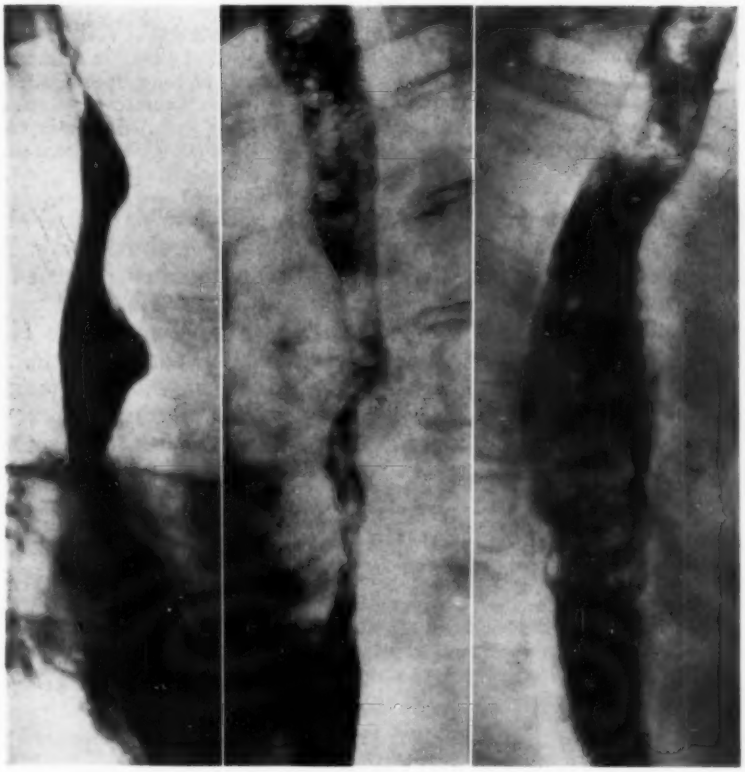


Fig. 9 a. 9 b. Fig. 10.

Fig. 9. Case 9. Carcinoma oesophagi. a. Ordinary contrast medium. A relative narrowing is seen at the level of the hila. b. Vigorous foam formation in involved area displaces contrast medium containing H_2O_2 in both directions.

Fig. 10. Case 10. Carcinoma oesophagi. Marked foam formation with regular large bubbles in contrast medium containing H_2O_2 in the dilated oesophagus.

Case 9. H. K., a female worker, aged 59. For almost two years vague pain in the chest, no typical difficulty in swallowing. Roentgen examination of oesophagus Dec. 1948 showed a narrowing of the oesophagus about 5 cm in length at the level of the pulmonary hila. With contrast medium containing H_2O_2 very distinct formation of foam was visible in the region and spread in both directions. A biopsy specimen was removed during oesophagoscopy. Pathological diagnosis: carcinoma spinocellulare. Died in local hospital in May, 1950 (Figs. 9 a and 9 b).

Case 10. M. T., a farmer's wife, aged 66. For some months previously the food seemed to stick in the throat and could only be swallowed after considerable mastica-

tion. Roentgen examination of the oesophagus, Feb. 1952: oesophagus dilatated evenly over its whole length. The junction of the middle and lower thirds of the left posterior wall did not seem to be quite smooth. The mucous relief was not clear. On administering a paste containing H_2O_2, vigorous foam formation occurred at the suspected area, and displaced the contrast medium. The appearances suggested an ulcerative process. Oesophagoscopy: a tumour is seen arising from the left posterior wall: it is lightly covered with mucous membrane and bleeds very easily. Pathological findings: carcinoma solidum (Fig. 10).

It is naturally too early to draw any conclusions as to the suitability of the method from the experiments, which number about forty. However, it seems probable that it could be developed so as to be used particularly when examining narrow passages. In theory it could perhaps be most easily adapted to the retrograde examination of the kidney (pyelography) but as yet this is hindered by the fact that the renal contrast media now in use consist of organic iodine compounds and do not permit of the addition of hydrogen peroxide. For this reason, research is being made into more suitable contrast substances for renal examinations. Experiments with barium contrast media are also being continued.

SUMMARY

The author presents a preliminary report on the visualization of ulcerative changes by using hydrogen peroxide in the contrast medium and describes preliminary experiments with a barium contrast medium containing this substance. The method is hardly of practical significance in the roentgen investigation of the stomach, although in the examination of the oesophagus and possibly, if a suitable medium can be found, in pyelography, it may prove to be of value.

ZUSAMMENFASSUNG

Der Verf. gibt einen vorläufigen Bericht über die Sichtbarmachung ulzeröser Veränderungen mit Hilfe von H_2O_2 im Kontrastmittel und beschreibt vorläufige Versuche mit Bariumkontrastmitteln, die diese Substanz enthielten. Die Methode ist für die Röntgenuntersuchung des Magens kaum von praktischer Bedeutung; jedoch kann sie für die Ösophagusuntersuchung und möglicherweise, wenn es gelingt ein brauchbares Mittel herzustellen, für die Pyelographie von Nutzen sein.

RÉSUMÉ

L'auteur présente une note préliminaire sur la visualisation des ulcérations grâce à l'emploi d'eau oxygénée dans le produit de contraste et décrit ses expériences préliminaires avec une bouillie barytée contenant cette substance. Cette méthode n'a guère d'intérêt pratique pour l'examen radiologique de l'estomac, bien que, pour l'examen de l'oesophage et peut-être, si on peut trouver un produit convenable, pour la pyélographie, elle puisse se montrer intéressante.

FROM THE DEPARTMENT OF SURGERY (DIRECTOR: PROFESSOR OLLE HULTÉN) AND THE DEPARTMENT OF ROENTGENOLOGY (DIRECTOR: PROFESSOR FOLKE KNUTSSON). UNIVERSITY HOSPITAL, UPPSALA, SWEDEN

ROENTGEN EXAMINATION OF THE DEEP RECTOGENITAL POUCH

by

Lennart Walldén

The most inferior part of the peritoneal cavity, the rectogenital pouch, generally forms a small 'fissuriform' space between the rectum and the intra-pelvic genital organs (Fig. 1). The lower margin ordinarily lies at about the level of the posterior vaginal fornix or the upper border of the prostate, although in this respect there is considerable latitude for variation. Sometimes, indeed, the pouch comes right down to the pelvic floor and may even protrude through it in hernial-like bulges. In special circumstances a deep rectogenital pouch may project into the vagina or the rectum, in which case the bulge is covered by the dorsal vaginal wall or the ventral rectal wall. When the protrusion presents through the anus the condition is known as true rectal prolapse.

In a recent publication (WALLDÉN, 1952) the author described some studies on the pathogenesis, clinical signs and roentgenology of the deep rectogenital pouch. The main theme of the investigation was the association between the anatomic anomaly and a defecation disorder, not previously investigated, the characteristic feature of which is a sensation that the rectum is blocked while straining at stool. On rectal palpation the examining finger feels, particularly during straining, the anterior rectal wall in such patients bulging down and thus obstructing the ampulla, in extreme cases down as far as the anorectal ring (Fig. 2).

While a deep rectogenital pouch may be an isolated anatomic anomaly, it may also be secondary to uterine prolapse or to ptosis of some other pelvic organ. Combinations of both types probably occur. The cause of a primary deep rectogenital pouch was previously a debatable question. In some cases the condition is ascribed to non-occurrence of the obliteration which normally takes place during the latter half of intra-

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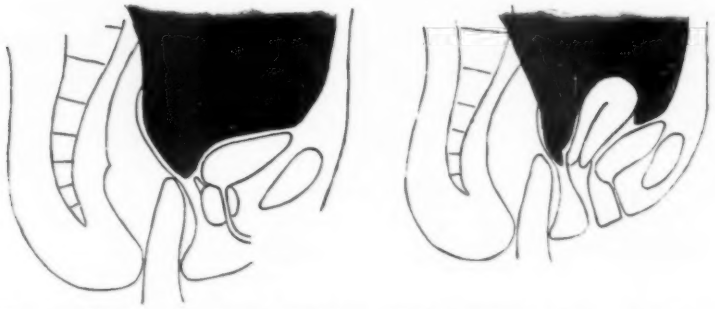


Fig. 1. Diagram showing the relations of the ventral rectal wall and the prostate or uterus, and of the rectogenital pouch, as felt per rectum.

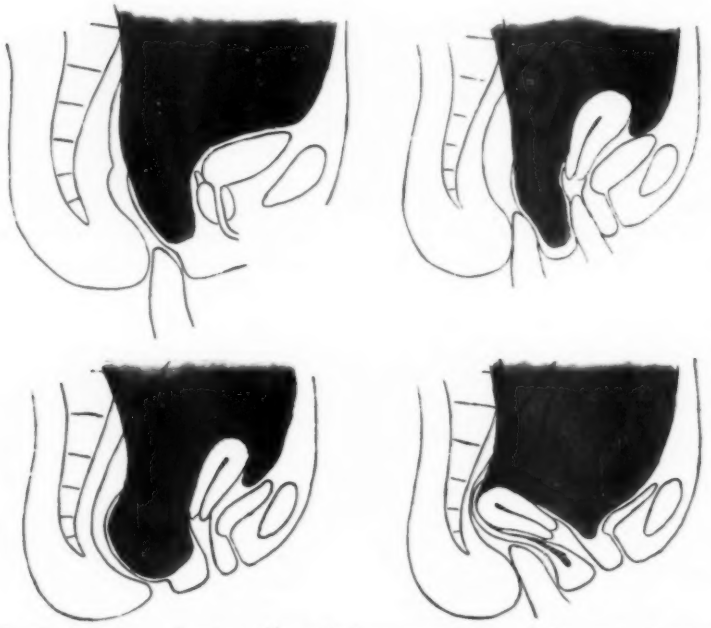


Fig. 2. Diagram showing the palpatory conception of the ventral rectal wall, the prostate or uterus and vagina, and the rectogenital pouch during straining in certain patients with defecation block.

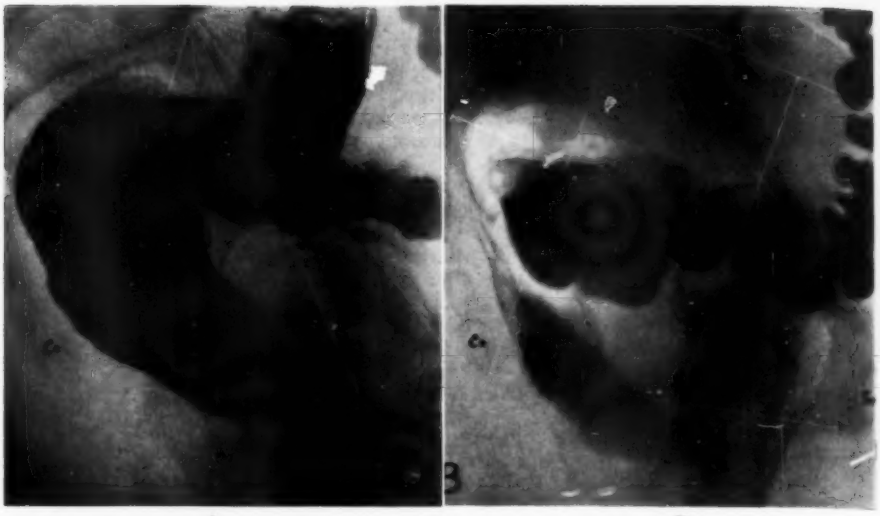
uterine life: up to that time the pouch is extremely deep. Some investigators, however, repudiate that such an obliteration occurs. Its existence is nevertheless confirmed by the author's observations in a series of 64 fetuses. The non-occurrence of obliteration theory is, moreover, supported by two 7—8 month fetuses in which a deep and wide rectogenital pouch had persisted. Published reports of cases of herniae from deep rectogenital pouchs in new-borns and several cases in the author's clinical series in which a deep rectogenital pouch was diagnosed during the growing period, also lend weight to the theory.

In the light of this interpretation one might draw a parallel between a congenital deep rectogenital pouch and a patent processus vaginalis peritonei. But just as the latter anomaly often is discovered only in the adult following the development of an inguinal hernia, a deep rectogenital pouch may remain latent until, filled with intestine, it gives rise to clinical signs or is disclosed on rectal palpation or roentgen examination. Such filling of the deep rectogenital pouch in young subjects takes place as a rule during straining only, while in older subjects it may be a fairly permanent condition. The size of the pouch and any secondary alterations of the topography of the pelvic organs are of course capable of wide variation, and in this fact one probably must seek an explanation for the varying lengths of time that elapse before the onset of clinical manifestations.

An appraisal of the anatomic background in the author's cases of defecation block was obtained by means of a special roentgen technique based on contrast medium introduced into the intestines in the true pelvis. This method, however, gives no direct information as to the extent of the pelvic peritoneal cavity. Only when the contrast medium extends markedly inferiorily is a conclusion justified concerning the depth of the peritoneal cavity.

Whether a deep rectogenital pouch be present or not, the pelvic peritoneal cavity contains not only loops of small intestine but the sigmoid colon and, in women, the uterus, the position of which may vary appreciably. The relations of these organs to one another varies from subject to subject and also from time to time in the same case. Hence it is not sufficient to study only the position of the small intestine in the true pelvis but an examination of the rectum and sigmoid colon by a barium enema must be included. Sometimes by collating these appearances, conclusions concerning the position of the uterus are possible. But the rectal films are most important in providing opportunities for determining the position of the pelvic floor and of estimating its displacement during straining. While a general estimation is obtained from certain landmarks on the pelvic skeleton, the caudal limit of the intestines in the true pelvis may best be evaluated through their relation to the pelvic floor.

The material comprised 12 men and 29 women — the series of defecation block — and was compared with a control series of 104 healthy subjects. The ages of the controls lay between 4 and 60. Since there proved to be a wide range of anatomic variation among the controls



A. B.

Fig. 3. Pelvis (lateral). A. Rectum filled with contrast for determination of the position of the anorectal ring — on relaxation. B. Rectum after evacuation of most of the contrast for determination of the position of the anorectal ring — on straining. (The white line between the tip of the coccyx [Co.] and the lower margin of the symphysis [Sy.] designates the median diameter of the pelvic outlet.)

with configurations verging on the pathologic and forms approximating to those of defecation block, it seemed essential to standardize the examination technique so as to make the films suitable for statistical analysis. This part of the investigation, one of the objects of which was to demonstrate and objectively to evaluate the difference between the two series with regard to the mean position of the intestines in the true pelvis, is described in the aforementioned publication. The measurements obtained are of considerable importance in the discussion of the principles in the main investigation. Yet they are of less interest in the present paper; the object is merely to give an account of the examination technique and to illustrate a few cases of deep rectogenital pouch regardless of the presence of clinical signs.

Examination Technique

After being directed to empty the bladder the patient is placed on a trochoscopy couch and given a barium enema as for an ordinary examination of the colon. When the contrast medium has reached the

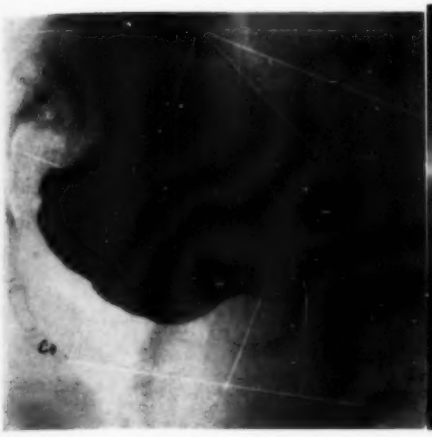


Fig. 4. Pelvis (lateral) with contrast in the small intestine, the lower margin of which is convex.

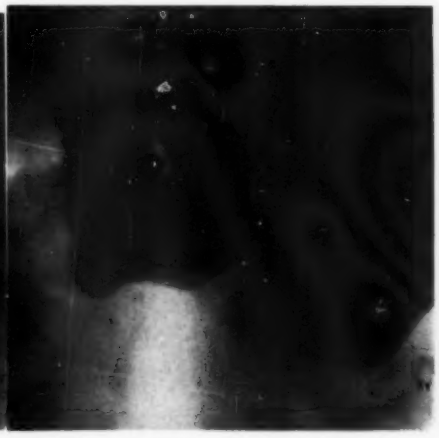
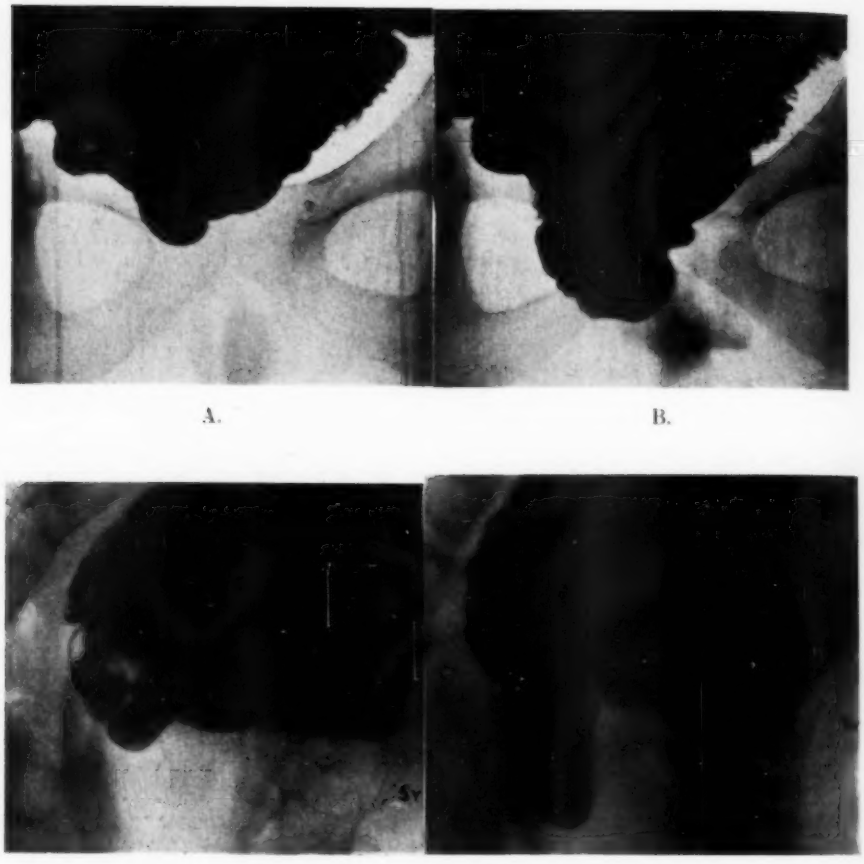


Fig. 5. Pelvis (lateral) with contrast in the small intestine, the lower margin of which is concave with a conical projection posteriorly; an incisura near the centre probably signifies the position of the uterus.

descending colon the enema is stopped. Lateral films of the pelvis (Fig. 3 A) are obtained with the central ray directed by fluoroscopy about midway between the ventral and dorsal skin surfaces at the level of the symphysis pubis, the patient standing with the arms crossed over the chest, the hip and knee joints extended and the heals against a straight edge fixed parallel with the central ray. Two post-evacuation films are obtained, also in the erect position, the second of these with the patient straining as much as possible in order to observe the effect of abdominal press on the position of the pelvic floor (Fig. 3 B).

When the barium enema has been completely evacuated and the rectum and sigmoid colon washed out, a barium meal is given as for an ordinary examination of the stomach; it is divided into two portions of about two ordinary glassfuls given at an interval of two hours. An hour after the last of the barium has been administered, the patient is directed to empty his bladder, and an exposure is made of the whole abdomen; this provides a general idea of the distribution of the contrast in the small bowel. After a single dose of barium, considerable variations in the transit times have been experienced. Less variation occurs, however, after the double administration as the second portion of barium accelerates the passage of the whole through the small intestine. When a survey exposure shows that the small intestine is regularly filled from



A. B.

C. D.

Fig. 6. Pelvis (a—p. and lateral) with contrast in the small intestine. A and C: on relaxation. B and D: on straining — the depressed contrast shadow on the a. p. view tapers below and on the lateral view is very narrow.

the stomach to the caecum, the patient is screened erect. Intense straining will be seen to displace the small intestine caudally while a relaxation of the straining permits its return to its original position. One a. p. and two lateral views are then obtained, the last film with the patient exerting maximal strain (Figs. 4, 5, 6, 7, 8 and 10), as for the examination of the rectum.

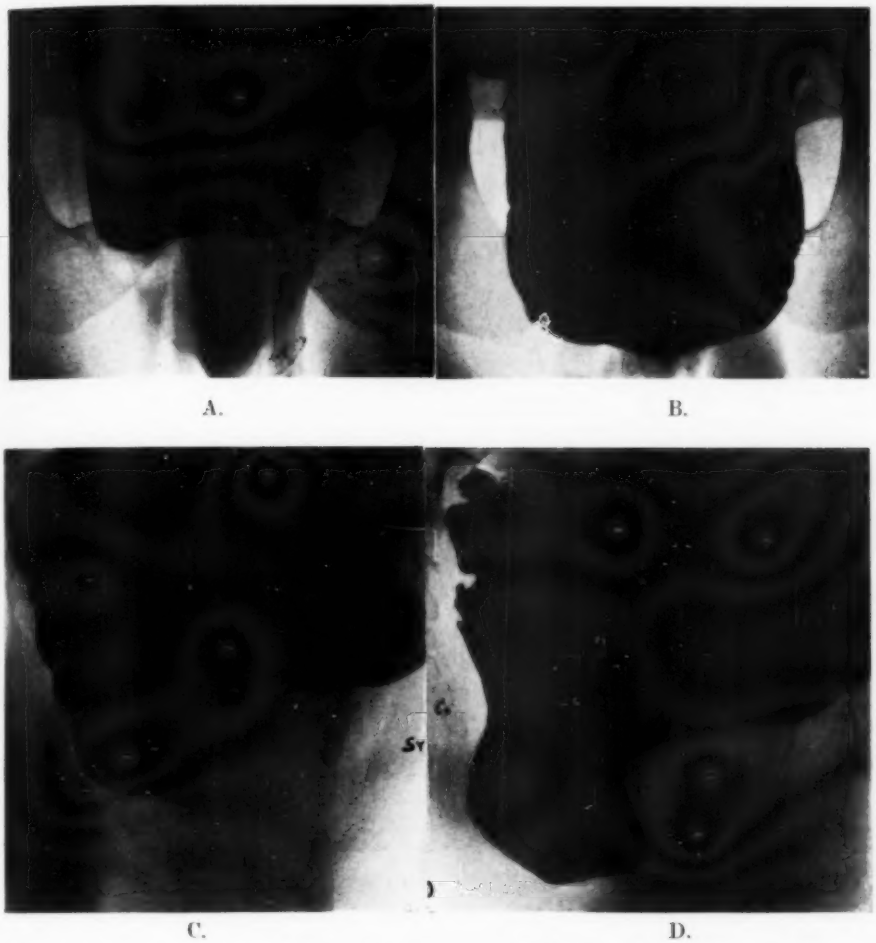
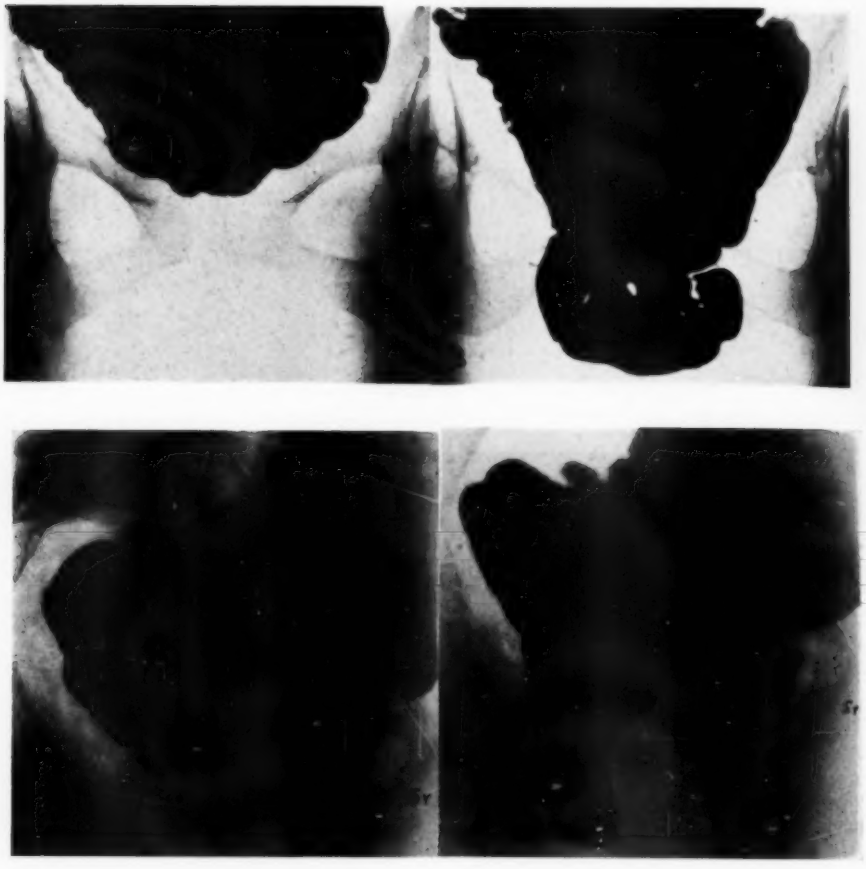


Fig. 7. Pelvis (a—p. and lateral) with contrast in the small intestine. A and C: on relaxation — the lower contrast margin is unusually low. B and D: on straining — the contrast shadow is depressed still further. In the a. p. view it is equilateral and in the lateral view slightly broader below than at the tip of the coccyx.

The Shape of the Rectum and the Position of the Pelvic Floor

In the lateral view the contrast in the rectum shows the degree of rectal curvature in the sagittal plane and the variations in the lower



C. D.

Fig. 8. A—p. and side views of pelvis with contrast in small intestine (a—p. and lateral). A and C: on relaxation — the lower contrast margin at a normal level. B and D: on straining — the depressed contrast shadow in the a—p. view is pear-shaped but in the lateral view tapers below.

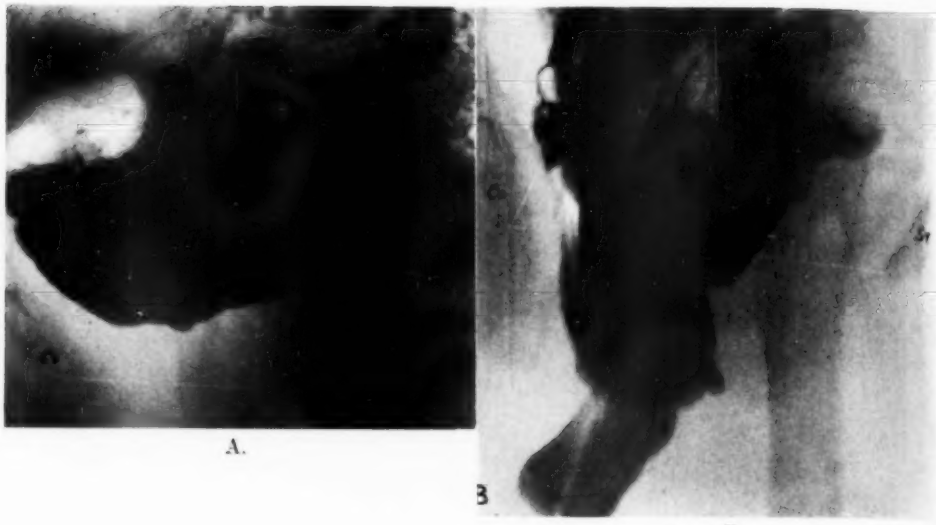
margin of the rectum. The latter represents the point where the rectum blends into the anal canal, the borderline being marked by the anorectal ring, of which a part is formed by the pars puborectalis of the levator ani muscle. By virtue of its central situation the anorectal ring may be regarded as indicating the position of the pelvic floor.

Fig. 9. Pelvis (lateral) after evacuation of most of contrast. A: on relaxation. B: on straining; the recto-sigmoid junction is displaced to the level of the coccygeal tip.

The anorectal ring in the child is situated comparatively antero-superiorily, making the part of pelvic floor posterior to it proportionately larger than in adults. During the growing period the anorectal ring is gradually displaced postero-inferiorily until, in the adult, it lies approximately in the middle of the median diameter of the pelvic outlet. Advancing age may apparently be accompanied by further postero-inferior movement. In about 50 per cent of males the rectum reaches below the pelvic outlet, while the corresponding figure for women is more than 80 per cent. This appears to be unaffected by the depth of the rectogenital pouch.

The position of the anorectal ring during relaxation is determined in films obtained with the rectum filled with contrast medium (Fig. 3 A), whereas the displacement during straining is studied after the evacuation of the barium enema from the small quantity which adheres to the walls (Fig. 3 B). Straining may possibly displace the contrast medium within the gut, but the closed anorectal ring prevents it entering the anal canal.

Such appearances provide a general picture of the individual variation of the position of the pelvic floor during straining and relaxation, and it is important that this factor be taken into account when evaluating the inferior position of the small bowel in corresponding circumstances.



A. B.

Fig. 10. Pelvis (lateral) with contrast in small intestine in a case of rectal prolapse. A: on relaxation — the caudal margin at a normal level. B: on straining — the small intestine and the prolapsed rectum are together displaced inferiorily far beyond the pelvic outlet.

Inferior Position of Intestine in the Pelvic Peritoneal Cavity

Films obtained after evacuation of most of the contrast medium from the rectum are sometimes of use for assessing the level of the intestine in the true pelvis: in certain cases the recto-sigmoid junction may be displaced down to the bottom of the rectogenital pouch during straining, and this in itself is enough to demonstrate the abnormal depth of the pouch (Fig. 9 B).

In a. p. views the small bowel shadow varies remarkably little when the rectogenital pouch is of normal depth. The inferior margin seldom reaches lower than the pars acetabularis ossis pubis. While the small intestine shadow may have a convexly rounded inferior contour in lateral views (Fig. 4), this contour is more often concave and, more or less like an inverted cone, projecting towards the pelvic outlet (Fig. 5). The extremity of the cone shows how far the small intestine reaches towards or into the rectogenital pouch. Both these appearances and transitions between them occur in men as well as women. During straining the small bowel is usually displaced down to, and sometimes beyond the pelvic outlet. The distance covered by, and the configuration of the

displaced small intestine contour vary; and, as noted, the limit of normal variation is wide. During childhood the small bowel most often lies more superiorily, but occasionally the inferior margin reaches, and during straining passes, beyond the pelvic outlet. In some women the inferior margin of the contour of the contrast has a definite incisura (Fig. 5), usually near the middle although sometimes more anteriorly and very occasionally somewhat posteriorly. This defect should make it possible to determine the approximate position of the uterus by which it is caused.

When the rectogenital pouch is abnormally deep the a. p. films display varying appearances. In young and middle-aged patients the inferior margin of the small intestine during relaxation usually lies more or less at the normal level, whereas during straining it is often displaced downwards, only to return rapidly to its original position when straining ceases. In elderly subjects, however, the small intestine generally reaches far inferiorily even when no straining is exerted. During straining the shape of the lowest contrast shadow which is displaced ranges from the inverted cone type (Fig. 6 B) through a more or less equilateral configuration (Fig. 7 B) to a pear-like shape (Fig. 8 B). Similar variations are found in the lateral views. In certain cases the displaced small intestine is seen to be very narrow (Fig. 6 D). In other cases it is wide superiorily and tapers down inferiorily (Fig. 8 D) and occasionally it is slightly broader below than above (Fig. 7 D) by reason of the fact that the tip of the coccyx makes a dorsal impression in its contour. The material also included numerous cases, however, in which the roentgen appearance, while not presenting such characteristic features, nevertheless disclosed the small intestine extending very low in relation to the pelvic floor. The diagnosis consequently cannot be based solely on the shape of the bowel but must also take into account the amount of intestine lying in the pelvic peritoneal cavity. In women, moreover, the uterus may be displaced backwards, sometimes creating a characteristic indention upon, but often completely masked by, the small intestine. In such cases hysterography may form a useful supplementary investigation.

The roentgenologic signs are confirmed by the anatomic findings on laparotomy. This was performed in 28 of the cases of defecation block. In the majority of instances the pouch not only proved abnormally deep but in addition was remarkably wide so that the rectogenital folds had vanished. Sometimes, too, the peritoneum in the wide pouch was wrinkled which further aided its extension downwards. Occasionally the deep pouch showed a distinct upper margin in the form of folds coming in from the sides and possibly interfering with the replacement of any intestine that might have entered the pouch during straining. The liter-

ature describes other cases in which the contents of such a hernial sac was retained so that obstruction, followed by gangrene of the bowel developed.

The extreme form of deep rectogenital pouch which constitutes true rectal prolapse may also be visualized by this method of examination, a fact which at least is of pathogenetic significance. Such a case is illustrated in Fig. 10 which shows that on relaxation the small intestine lies on a normal level in the pelvis but on straining is depressed downwards together with the prolapse far beyond the pelvic floor.

SUMMARY

The rectogenital pouch may be very deep and take the form of a hernia through the pelvic floor. The deep pouch and its contents may also bulge against the rectum or vagina, through which, in extreme cases, they may present. Pressure on the rectum sometimes causes a defecation disorder characterized by obstruction. The anatomic deviation may be visualized by the roentgen examination of the pelvis after a suitable contrast medium has been introduced into the intestines contained in the pelvic peritoneal cavity. The technique of such an examination is described and the typical appearances are illustrated.

ZUSAMMENFASSUNG

Die Excavatio recto-genitalis kann sehr tief sein und die Form einer Hernie durch den Beckenboden annehmen. Die tiefe Ausbuchtung und ihr Inhalt kann auch gegen das Rektum und die Vagina hervorbuchten, durch welche sie, in extremen Fällen, sichtbar sein kann.

Der Druck auf das Rektum erzeugt mitunter Defäkationsbeschwerden, die durch Obstruktion karakterisiert sind. Die anatomische Abweichung kann durch Röntgenuntersuchung des Beckens nach Einführung eines geeigneten Kontrastmittels in die das Becken ausfüllenden Därme sichtbar gemacht werden. Die Technik einer derartigen Untersuchung wird beschrieben und typische Bilder werden gezeigt.

RÉSUMÉ

Le cul-de-sac génito-rectal peut être très profond et prendre la forme d'une hernie à travers le plancher pelvien. Ce cul-de-sac profond et son contenu peuvent aussi bomber dans le rectum ou le vagin, à travers lesquels ils peuvent, dans les cas extrêmes, se présenter. La pression sur le rectum cause parfois un trouble de la défécation caractérisé par une obstruction.

La déviation anatomique peut être mise en évidence par l'examen radiologique du bassin après opacification convenable de l'intestin contenu dans la cavité péritonale pelvienne. La technique de cet examen est décrite et les images typiques sont présentées.

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THE ROENTGENOLOGIC APPEARANCE OF THE AQUEDUCT OF SYLVIUS

by

E. Lindgren and *G. Di Chiro*

The Normal Aqueduct

The normal aqueduct of Sylvius appears in lateral encephalograms as a narrow channel connecting the third and fourth ventricles. This channel is generally considered to have a smoothly curved course from the posterior lower part of the third ventricle to the fourth ventricle (LYSHOLM, ROBERTSON, SUTTON). DAVIDOFF and DYKE, however, describe its course as follows: "In its anterior half the aqueduct courses almost horizontally but at its mid-portion it curves sharply inferiorly, becoming almost vertical."

In our experience none of the descriptions is true of the aqueduct in general for the appearance, in fact, is not the same in every case. In some instances the aqueduct forms a gentle arch. This was encountered in about 35 % of a series of 300 encephalograms performed in our department. In the majority of cases, however, (about 65 per cent) the aqueduct formed various angles. DAVIDOFF and DYKE probably made similar observations and their description referred to the latter type. In cases where the cisterna venae Galeni is filled by air at the same time as the aqueduct, the anatomic correlation between the aqueduct and the quadrigeminal plate can be assessed. The aqueduct reaches as far as the quadrigeminal plate, which forms its upper dorsal border. The angle of the aqueduct appears to correspond with the border between the superior and inferior colliculi. In some cases the floor of the aqueduct has a smoothly curved course while the roof is angulated to a degree depending upon the shape of the quadrigeminal plate; a slight widening at the level of the apex appears, and it seems to us as if this widening

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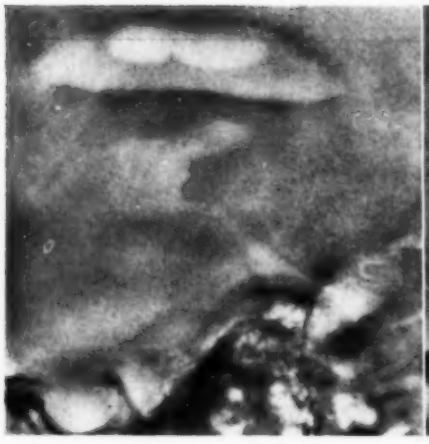


Fig. 1. The kink of the normal aqueduct. Note that at the level of the kink there is a slight widening ('ventriculus mesencephali' of Retzius).

Fig. 2. Another case of kink of the normal aqueduct; the aqueduct is somewhat narrower at the level of the kink.

is what RETZIUS has referred to as the 'ventriculus mesencephali'. In other cases the floor and the roof run parallel and thus there is a real kink — the kink of the normal aqueduct. In most instances this kink is not prominent and causes no differential diagnostic difficulties; occasionally, however, the kink may be so marked that it has exactly the same appearance as the aqueduct when an expanding lesion in the posterior fossa is present (fig. 1, 2). At first the shape of the aqueduct would appear to be closely allied to that of the posterior fossa, the kink being more marked in a short posterior fossa, but we have not found any relation between the degree of sharpness of the kink and the shape of the skull. The kink of the normal aqueduct is recognisable in encephalograms of patients of all ages.

Various authors who have carried out measurements of the aqueduct, differ in their opinions. SAHLSTEDT (1935) gave a length of 2 cm and CARILLO (1937) of nearer 3 cm. DAVIDOFF and DYKE (1939), ROBERTSON (1941) and SUTTON (1950) stated in agreement that the aqueduct of Sylvius, as shown by pneumography, measures about 1.5 cm in length. In 1950, however, EPSTEIN stated that the average length of the aqueduct was 3 cm. It seems unlikely that the marked differences in the measurements reported could depend on variations in the focus-film distances used for the encephalograms from which the measurements were obtained. The disparity in the given figures must therefore be accounted for in

Fig. 3. Simultaneous airfilling of the aqueduct and of the cisternal space above the quadrigeminal plate. Length of the aqueduct 1.8 cm.

Fig. 4. The widening (arrow), which sometimes marks the end of the aqueduct and the beginning of the 4th ventricle. Length of the aqueduct 1.8 cm.

another way. Either the technique employed is such that the shape of the aqueduct is not accurately reproduced in the films, or the choice of landmarks for the measurements has varied. The technique used for the representation of the aqueduct also affects the appearance of the kink, which is, in many cases, so slight that it has to be demonstrated in a true lateral projection in order to be assessed. Even a small degree of deviation of the central roentgen ray upwards or downwards can make the kink disappear partly or completely from the film. Forward or backward deviation of the beam causes an inaccurary in the apparent length of the aqueduct. No positioning, involving turning of the head, can be sufficiently exact for the precise judgement of the shape of the aqueduct. The authors' examinations are thus solely based upon films obtained with the patient in the sitting position, the rays being horizontal with the central beam directed approximately over the site of the aqueduct. The upper limit of the latter may be fairly easily recognised. For purposes of measurement one may choose, as the upper landmark, either the most anterior point of the bulge made in the third ventricle by the posterior commissure (we used this point in carrying out our measurements), or the point at the level of the mouth of the aqueduct where there is (by no means constantly) a slight narrowing due to the posterior commissure. As a matter of fact the two points are so close to each other that the choice between them, for measurement purposes, is of very

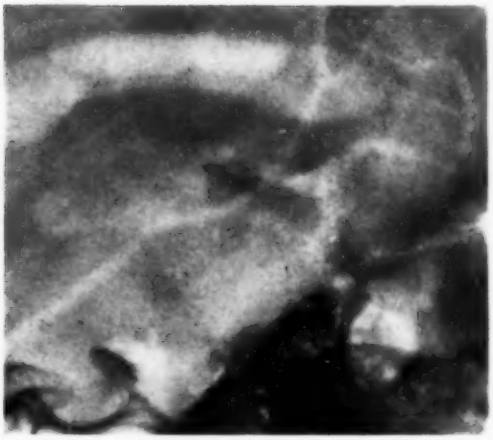
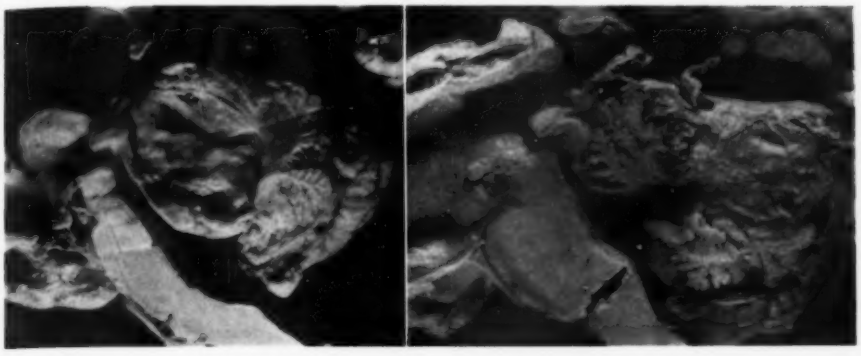


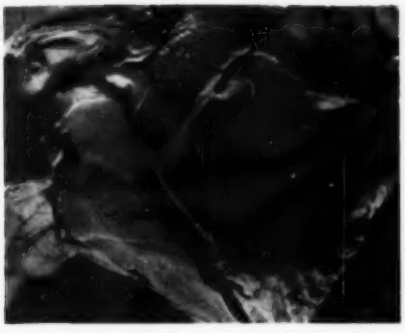
Fig. 5. Simultaneous airfilling of the aqueduct and of the cisternal space above the collicular plate. Note that the widening we use as the inferior landmark in the measurement of the aqueduct corresponds with the lower border of the midbrain.

Outline of Fig. 5.

little significance. The identification of the inferior landmark is much more difficult. It is not easy to assess where the aqueduct ceases and the fourth ventricle begins. The authors who have given the figure of 3 cm have very probably included a part of the fourth ventricle in their measurements. The lower end of the aqueduct is marked by the lower border of the collicular plate. It is therefore clear that we have an indirect but precise method of measuring the length of the aqueduct when a simultaneous airfilling of the aqueduct and of the cisterna venae magnae cerebri, outlines the quadrigeminal plate. We made such measurements in 30 cases and found that the length of the aqueduct was nearly constant between 1.6 and 1.8 cm (the latter figure occurring more frequently). Occasionally the aqueduct is somewhat longer — 1.9 cm. In only one case among the 30 measured, was the length of the aqueduct 1.5 cm. The anatomic length of the aqueduct is generally said to be 1.5 cm or a little less. Our figures correspond well with this anatomic length, when the enlargement obtaining with a focus-film distance of 70 cm (Lysholm skull table) is taken into consideration. Our figures correspond mostly, therefore, with the findings of DAVIDOFF and DYKE, ROBERTSON and SUTTON. This suggested method for measurement of the encephalographic length of the aqueduct is but indirect. There is, however, in some cases, the possibility of assessing the lower



a. b.



c.

Fig. 6. Three cases of cerebellar lesions producing the typical pathologic kink. The bend of the collicular plate is situated between the superior and inferior colliculi.

end of the aqueduct in a direct way, even when only the aqueduct is air filled. The border between the aqueduct and fourth ventricle is, in certain cases, sharply delineated at the junction of the anterior extremity of the superior medullary velum with the quadrigeminal plate. In some cases a small, angular bulge originates in this region, quite close to the lower border of the quadrigeminal plate (figs. 4, 5, 7). In nine cases this border could be seen distinctly and the length of the aqueduct thus measured directly. By this method the aqueduct was found in the films to have the following measurements: 1.7 cm in two cases, 1.8 cm in six cases and 1.9 cm in one case. These figures correspond with those obtained by the indirect method.

The Pathologic Aqueduct

For rather a long time a kink of the aqueduct has been considered to be pathognomonic of a tumour in the posterior fossa (TWINING, LYS-

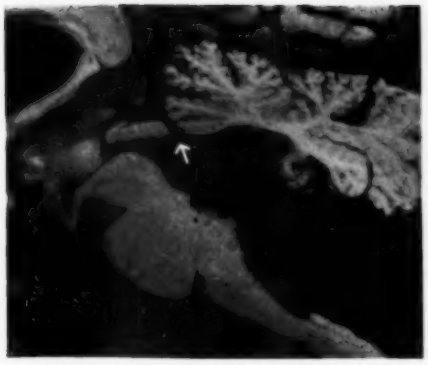


Fig. 7. Case of sub-fastigial lesion. Note that the widening at the level of the upper angle of the 4th ventricle (in normal cases, slight) is here prominent (arrow).

Fig. 8. Another case with a marked widening of the angular bulge at the border between the quadrigeminal plate and the fourth ventricle in a case of a tumour of the lower part of the 4th ventricle.

HOLM, HYNDMAN, a. o.). From what has been said above, this alone is not quite true. LYSHOLM stated that the kink is situated in the supratentorial part of the aqueduct, while TWINING preferred to call it the pertentorial portion. It is not always possible to decide which is the case by a pneumographic examination, as the anterior edge of the tentorial portion is not, as a rule, clearly visible. This edge is not distinct in the midline, but curves upwards and passes over into the falx. These opinions seem, to us, to be of little value. Since in many cases the normal aqueduct has a certain degree of kink, the question arises whether that, which may occur in infratentorial expanding lesions, is an accentuation of the normal or if it is situated in an abnormal location. It is evident, from films published by TWINING, that the former is the fact in at least some cases. It appears, from all our cases examined both by encephalography and patho-anatomic investigation, that this pathologic kink generally is nothing else but an accentuation of the normal appearance (fig. 6). This finding is illustrated most obviously in tumours of the vermis, especially if situated in its upper part. The aqueduct is angulated and the walls are almost parallel down to the constriction which may occur. If the tumour be situated in the lower part of the vermis, or in the fourth ventricle, various changes may occur. If the tumour be situated so that the fourth ventricle is dilated without being displaced, no kink

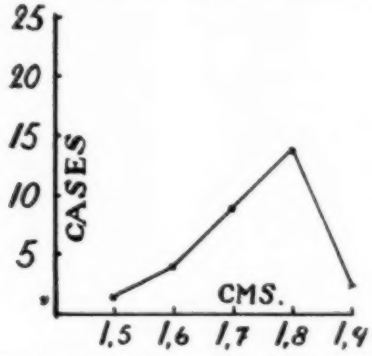
Fig. 9. The entire aqueduct is pushed forwards by a tumour in the tentorial slits (meningioma). The shape of the quadrigeminal plate is unchanged. The compression of the aqueduct commences below the plate.

Fig. 10. Glioma of the quadrigeminal plate. Straightening of the aqueduct, which has irregular borders. The angular bulge is evident.

as a rule appears. Instead, the quadrigeminal plate will be straightened out and its lower dorsal part will be displaced upward. The aqueduct will be dilated to the shape of a funnel down to the fourth ventricle (fig. 7), possibly to such an extent that the floor of the fourth ventricle is flattened and displaced forward. If the tumour be situated more in the lower part of the fourth ventricle, so that this is pushed upward, the quadrigeminal plate may retain or increase its angulation, even in those cases in which the lower dorsal part of the quadrigeminal plate is displaced upwards causing a widening of the aqueduct. In these cases, when the upper part of the fourth ventricle is dilated, the angular bulge at the border between the quadrigeminal plate and the fourth ventricle will be considerably widened and completely lose its original shape (fig. 8). The quadrigeminal plate then appears more clearly defined than is otherwise the case. However, in tumours high up in the posterior fossa, especially those situated in the tentorial slits, the whole aqueduct will be displaced considerably forwards. It is only in these circumstances that the kink is not found in its usual situation in the middle part of the quadrigeminal plate; the latter becomes straight and turns, in its entirety, forwards and downwards so that the kink which arises is situated at the upper point of the quadrigeminal plate on the border of the third ventricle (fig. 9).

The statements above concern tumours which do not directly infiltrate the quadrigeminal plate. Tumours of the quadrigeminal plate

are very rare and experience of these is therefore limited. In the cases we have seen the quadrigeminal plate has been more or less straight (fig. 10). It has been thickened and, because of that, the aqueduct has had a more vertical course, reminding us of its appearance in a tumour



Graph showing length of the aqueduct in 30 cases as measured by the indirect method (simultaneous airfilling of the aqueduct and of the cisterna venae magnae Galeni so that the quadrigeminal plate is outlined by air).

of the tentorial slits. It seems to be of value in the differential diagnosis that, in the presence of a displacement of the quadrigeminal plate, the wall of the aqueduct is smooth and the border between the third ventricle and the aqueduct has a normal appearance. In tumours of the quadrigeminal plate the border of the aqueduct becomes irregular and, if the upper part of the plate be thickened, changes the appearance of the dorsal part of the third ventricle.

Conclusions

The shape of the aqueduct thus seems to be dependent upon the anatomic shape and the position of the quadrigeminal plate. This plate is rather resistant to pressure and the deformity sustained is therefore small. In expanding lesions behind and beneath the quadrigeminal plate, the aqueduct becomes kinked at the weakest situation, *i. e.* the border between the inferior and superior colliculi. In expanding lesions, situated so that they only cause a widening of the fourth ventricle, the plate will turn backwards and upwards, in its entirety, with or without retaining its normal angulation, and consequently the aqueduct will be dilated. Expanding lesions situated behind and above the quadrigeminal plate, will tip the latter forwards.

SUMMARY

The course and shape of the normal aqueduct of Sylvius are first discussed and as a result of experiences gained in 300 encephalograms it is shown that the general descriptions commonly accepted require modification. The second part of the paper deals with the principles regarding deformities of the aqueduct in various situations of an expanding lesion in the posterior fossa.

ZUSAMMENFASSUNG

Der Verlauf und die Form des normalen Aquaeductus Sylvii werden im ersten Teil besprochen und als Resultat der aus 300 Enzephalogrammen gewonnenen Erfahrungen wird gezeigt, dass die gewöhnlichen Beschreibungen, die allgemein acceptiert sind, eine Änderung bedürfen.

Der zweite Teil behandelt die charakteristischen Veränderungen des Aquäduktes bei verschiedener Lage eines expansiven Prozesses in der Fossa posterior.

RÉSUMÉ

Les auteurs étudient d'abord le trajet et la forme de l'aqueduc de Sylvius normal et, se basant sur l'examen de 300 encephalographies, montrent que les descriptions générales communément acceptées doivent être retouchées.

Le deuxième partie de l'article donne les caractéristiques des déformations de l'acqueduc suivant le siège d'une lésion expansive dans la fosse postérieure.

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FROM THE ROENTGEN DEPARTMENT (DIRECTOR: HANS SAHLSTEDT),
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INTERNAL UTERINE ENDOMETRIOSIS

Report of two cases

by

Bengt Liliequist

Clinical diagnosis of internal uterine endometriosis is frequently difficult. Neither the clinical picture thereof with haemorrhage and pain, nor the palpation of an enlarged uterus can be regarded as diagnostic. The most important symptom, the increased and prolonged bleeding, may be explained by other changes in the uterus; *e. g.*, metropathia haemorrhagica cystica, myoma, or in the case of irregular or continuous bleeding by benign or malignant tumors. A specimen which permits of a positive microscopic diagnosis may sometimes be obtained on curettage, although the result is generally negative. Hysterography, however, produces a definite diagnosis in that it presents a characteristic picture. This was first described by ÅKERLUND in 1942. As this diagnostic aid in internal endometriosis appears, judging from the literature, to be little known, I feel justified in reporting two cases in which the diagnosis was based upon hysterography alone.

Case Reports

Case 1. The patient, a 53-year-old nullipara, had normal menstruation until one year before examination. During the previous year she had had two periods of very copious and painful vaginal bleeding of one month's duration, occurring with intervals of several months. Palpation revealed a firm and myomatous uterus, larger than the size of a fist.

Hysterography (fig. 1) showed a medium large, considerably retroflexed uterine cavity without a constant filling defect and with elongated tubal angles. The tubes were only partially filled and appeared to be of normal width. To the left of the uterine cavity, a large conglomerate of irregular ducts and smaller cavities was filled.

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Fig. 1. A conglomerate of irregular ducts, filled with contrast medium, arises from the left posterior part of the uterine cavity.

Little material was obtained by curettage and no diagnosis was possible. On further hysterography the same results were obtained as at the earlier examination; supravaginal hysterectomy therefore was performed.

On operation the uterus was found to be somewhat larger than fist-sized, very firm, and regularly rounded. The ovaries were small and rather fibrous.

In the hope of obtaining possible confirmation of the hysterographic observations, 10 ml of methylene blue solution were injected into the cervical canal. When the preparation was subsequently sectioned it was seen that the stain had penetrated a tree-like branching of fine ducts within an area approximately three centimeters in diameter, situated in the isthmus of the uterus. This region, which was considerably firmer in consistency than the rest of the myometrium, was not sharply defined.

There were several firm intramural myomata, ranging in size up to a golf ball, in the uterus. The endometrium was normal. The myometrium was generally hyperplastic with small passages between the fibromuscular bundles. These formations emptied into small pores in the endometrium. The myomata on the surface of the section showed severe hyaline degeneration, were highly differentiated and of benign appearance. In the rest of the uterine wall were numerous, in part somewhat cystic, foci of internal endometriosis.

Case 2. A 46-year-old nullipara reported normal menstruation until the age of 40, when gradually increasing menstrual bleeding without noteworthy pain began. On admission the patient was pale and short of breath after 14 days of copious bleeding. Palpation of the abdomen revealed that the uterus was considerably enlarged, firm and nodulous. There was abundant, foul-smelling bleeding into the vagina.

Currettage yielded moderate material but no diagnosis was possible.

Fig. 2. Large, irregular uterine cavity, from the upper part of which several contrast-filled canals arise.

Hysterography (fig. 2) revealed a rather large, irregularly formed uterine cavity with a roughly rounded filling defect bulging inwards from the left. From the upper margin near the right tubal angle, a considerable quantity of contrast medium passed into a network-like system of passages of varying width and length.

Supravaginal hysterectomy was carried out. Both tubes were rather thickened, occluded at their abdominal ends and somewhat adherent to the ovaries; these were in turn adherent to the lateral pelvic wall.

The uterine cavity was filled with methylene blue solution, and after section a myoma-like formation with numerous spaces filled with methylene blue solution was seen in its upper portion, principally to the right; the endometrium was normal.

Discussion

Endometriosis is a condition in which endometrial tissue grows outside the anatomic limits of the endometrium. This tissue and the uterine mucosa are histologically identical in their composition of characteristic glands and surrounding highly cellular stroma and in their partially menstrual and decidual capacity for reaction.

Internal uterine endometriosis is entirely limited to the uterine wall, where the glandular tissue with surrounding stroma grows diffusely into the musculature. This is a case of a locally destructive growth, in which the highly cellular stroma disperses and destroys muscle fibrils and connective tissue and may also invade lymph vessels; it closely resembles the behavior of malignant tumors. In the present instance, however,

the glandular tissue exhibits no signs of malignancy, the growth is locally defined and its expansion controlled by the hormonal influence of the ovary. The expansion ceases after the menopause. Endometriosis may be observed in all stages of transition, from the post-menstrual normal regeneration phenomenon in the mucosa to pronounced internal endometriosis; this latter condition is believed to be an intermediate stage between degenerative hyperplasia and blastomatous growth.

Macroscopically, the uterus is enlarged — it may be as large as a child's head. Its consistency is hard. As myomata frequently occur concurrently, the surface of the uterus may feel nodulous on palpation; this, however, often happens in the presence of cysts, which readily occur in abnormally situated endometrial tissue. Microscopic examination reveals wide glandular zones with surrounding highly cellular stroma originating from the basal parts of the uterine mucosa. These are interspersed in irregular bands in the musculature of the uterine wall. The lumina of the glands and the passages in the glandular zone may vary in size; their anatomic relation with the uterine mucosa can be demonstrated microscopically. This entire system of passages, sometimes ending in cystic spaces, is thus more or less connected with the uterine cavity and a suitable contrast medium injected into the uterus may fill it and be demonstrated roentgenographically. GOLDBERGER, MARSHAK and HERMEL consider this true in only about 15 per cent of cases. The reason why the contrast medium does not always fill the passages may be due to their being blocked by coagulated blood or to muscular hypertrophy constricting the passages. It may also be caused by the use of a contrast medium which is not free-flowing. The water-soluble contrast media are therefore more suitable than the iodized oils. Umbradil-viscous (Astra) was used in the two cases reported here; it penetrated and filled the system of passages without difficulty.

AKERLUND describes marked irregularities of outline as characteristic of the roentgenologic changes. These seem to consist principally of short narrow, contrast-filled bulges of rounded, oval, more elongated form from the uterine cavity. These sometimes occur so densely that the appearances simulate diverticulosis. MADSEN has described the manner in which, in internal endosalpingiosis, a long section of the tube is transformed into a network of paratubal passages. As in the two cases reported here, these may be tortuous and branching and a centimeter in length. They may frequently be seen arising from the fundus of the uterus.

SUMMARY

Two cases of internal uterine endometriosis diagnosed hysterographically are described.

ZUSAMMENFASSUNG

Zwei hysterographisch diagnostizierte Fälle von Endometriosis uteri interna werden beschrieben.

RÉSUMÉ

Présentation de deux cas d'endométriose utérine interne diagnostiqués par hystérographie.

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FROM THE ROENTGEN DEPARTMENT (DIRECTOR: PROFESSOR K. LINDBLOM),
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A RELEASE MECHANISM FOR RADIOGRAPHIC EXPOSURE GIVING IMPROVED PROTECTION OF PERSONNEL

by

Ove Mattsson

The regulations and recommendations for radiographic work which exist in every country define certain maximum dosages of radiation per unit of time to which personnel employed in radiographic departments may be exposed before their health becomes endangered. These maximum figures vary a great deal but are on a fairly low level.

According to GLOCKER (1950) the maximum dose allowed in Britain is 0.50 r per week and in U.S.A. 0.30 r. In Germany the figure is 0.25 r per day if the reproductive organs be protected. The value given by the International Commission on Radiological Protection (at the Sixth International Congress of Radiology, London, 1950) was 0.3 r (in air) per week (0.5 r on body surface). STONE (1952) has recently reviewed historical data and details on radiation injuries, estimations of tolerance doses and protection recommendations. In Sweden the maximum dosage allowed is considerably smaller and a more serious view is taken of the risks of radiation (HELDE 1946, SIEVERT 1947, WAHLBERG 1950 and others). The Institute of Radio-Physics at the Karolinska Sjukhuset, Stockholm, has given a very low figure, namely *0.1 r a week*. The regulations contain strict instructions for safety arrangements (built-in protection, lead screens etc.) and a working routine devised to protect against radiation is necessary under the Swedish Roentgen Ray Law of 1941. The protection measures

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used at present in Sweden partly correspond to those described by ÅKERLUND in 1935.

Swedish radiologists normally do not use lead rubber aprons during screening, but instead there are a great number of stationary protective arrangements. A certain amount of radiation, however, is inevitable in diagnostic work; secondary radiation, which may be diffused over the whole of the radiographic room always affects the personnel to a smaller or larger degree. Stray radiation in screening has been measured by COWING and SPALDING (1949), GLOCKER (1950), JACOBSSON, SCHWARTZMAN and HEISNER (1952) and others: it shows values which cannot be ignored.

Even though the smallest necessary primary diaphragm be used, large amounts of secondary radiation are produced during the exposure. In Sweden the tube and lead glass screen are frequently not coupled, and a considerable amount of direct radiation may thus emanate. In some examinations, such as bronchographies and the more and more frequent angiographies, the personnel must remain in the immediate vicinity of the patient, and a certain degree of protection is then afforded by aprons etc. This may of course also obtain when difficult children or adults are examined. The same is the case in spot film radiography, when screening and exposure follow immediately after one another. The radiation occurring in such cases was investigated by MORGAN (1949), based on American conditions. In the majority of examinations, the presence of personnel in the radiographic room during the exposure is not required, and it is of course very important that those in attendance on these occasions, particularly the operator in charge of the screening, should remain in the protected control panel room and exclude the radiation by closing the lead-covered door in accordance with Swedish routine. This is of special importance when large primary diaphragms are used. Urographies are considered to be particularly dangerous and this is also true of tomographies in which the motion of the tube causes a marked spread of the beam of radiation.

In mass radiography the amount of radiation is considerable. Protection problems in connection with photo-fluorographic equipment have been discussed by MORGAN and LEWIS (1946). The latest models of Swedish apparatus are protected by a lead plate hood accommodating patient and apparatus, and is completely closed during the exposure.

Radiation reaches the personnel during screening and during exposure. Because of the low values of the doses permitted and the considerable quantity of radiation which escapes from the radiographic equipment, all possible arrangements must be made to prevent unnecessary effects of radiation upon the personnel especially in departments with high working intensity. A reduction of the radiation danger during the actual exposure

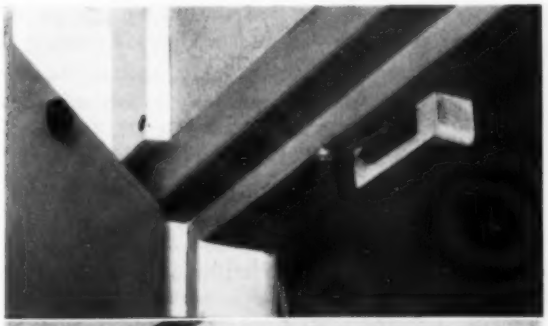

Fig. 1.

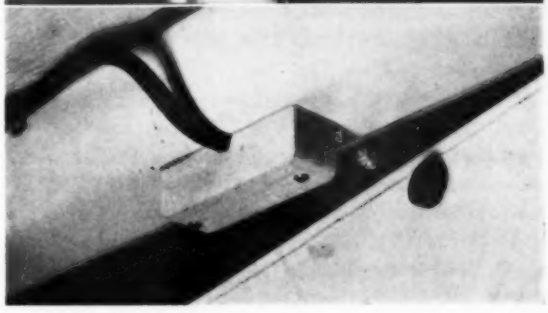

Fig. 2.

Figs. 1 and 2. The release mechanism controlled by the movement of the door of the protected control room. A rubber buffer on the door acts on a movable arm with a roller attached to a switch.

is no doubt a great advantage. It is the usual routine in Sweden that the radiologist and other personnel leave the radiographic room during every radiographic exposure. Departments are therefore nowadays planned in such a manner that both the vertical stand and the horizontal table are placed close to the door of the protected control room. This arrangement, however, permits considerable amounts of radiation to escape from the radiographic room if the door be not completely closed. Furthermore, there is also a tendency to make the radiographic rooms smaller, which increases the radiation risk (CHAMBERLAIN 1932). The exposure is usually made by an assistant as soon as the operator has given the command: "Hold your breath" and closed the door, but it may easily happen that it is made while the door is ajar. Many installations demand a certain time-lag to secure full rotation of the anode of the tube, and this fact increases the possibilities of exposure at an unsuitable moment.

Although loudspeakers are fitted to some units in Sweden for skeletal

radiography in order to facilitate instructioning the patient to hold his breath, the personnel frequently is careless about closing the door.

Exposures at an unsuitable moment, *e. g.* before the staff is protected can be prevented by a blocking arrangement which prevents any exposure as long as the room-door is not properly closed. Such devices have been used in connection with mass radiography, industrial radiography and in roentgen therapy. The author has designed a release mechanism, which not only acts as a blocking device but also releases the exposure automatically at the correct moment when the door has been completely closed. It consists of a switch controlled by the position of the door, and closes a circuit connected to the control panel in such a manner as to actuate the timer. The exposure is thus blocked until the switch is engaged, but it can at will also be released by a normal exposure manipulation, if the door has first been closed.

The arrangement secures improved protection of personnel and ensures quicker working, because the door will never have to be closed other than at the very instant of exposure. Its value for skeletal radiography is obvious. In screening, the exposure is released by the examiner through the motion of the door and the nurse is relieved of watching the door and of deciding the appropriate moment of exposure. The work of the examining radiologist is also facilitated as the instant of exposure is entirely under his control.

The appearance of the apparatus is shown in Figs. 1 and 2. A rubber buffer on the door acts on a movable arm with a roller which is attached to the switch. When the door is closed the switch completes the circuit controlling the exposure. Every radiographic camera can be equipped with this releasing mechanism. The device shown in Figs. 1 and 2 was fitted to an installation in which the roentgen tube was directed against the protection door itself and in which the lead glass screen was not directly coupled with the tube so that direct radiation from the latter could reach the doorway, especially when large diaphragms were used, *e. g.* in chest radiography.

A by-pass arrangement is fitted which cuts out the release mechanism and permits if necessary normal manipulation from the control panel.

The installation has served well for several months and the staff finds it quite convenient.

A regular check of the function of the switch is necessary so that any adjustments required may be made.

SUMMARY

In order to reduce the danger of radiation associated with the radiographic exposure, the author has designed a release mechanism controlled by the movement of the door of the protected control room. In this manner the personnel is fully guarded against the radiation and the instant of exposure is kept under the radiologist's control.

ZUSAMMENFASSUNG

Zur Verringerung des Strahlenrisikos bei Röntgenexponierungen hat der Verf. einen Auslösungsmechanismus konstruiert, der durch das Schliessen der Tür zum strahlengeschützten Manöverzimmer beeinflusst wird. Exponierung geschieht also nur dann, wenn das Personal geschützt ist und der Untersucher hat den Auslösungsmoment völlig in seiner Hand.

RÉSUMÉ

Pour réduire le danger d'exposition aux rayons pendant la prise des radiographies l'auteur a conçu un mécanisme de déclenchement actionné par le mouvement de la porte du poste de commande. Le personnel est ainsi complètement à l'abri des rayons et le moment de la prise du cliché reste sous le contrôle du radiologiste.

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A TIME-PICTURE RELATION STUDY WITH AUTORADIOGRAPHY ON THE UPTAKE OF LABELLED SULPHATE IN THE GRAAFIAN FOLLICLES OF THE RABBIT

by

Erik Odeblad and *Harry Boström*

In an earlier paper (BOSTRÖM and ODEBLAD 1952) we have shown that the follicular fluid takes up considerable amounts of labelled sulphate, whereas the cells of the stratum granulosum retain only small quantities. It was demonstrated in a subsequent study (ODEBLAD 1952, I) that a close relationship exists between the amount of dry substance, the presence of metachromasia and the incorporation of radiosulphate in the follicular fluid. As, however, the mechanism by which the sulphate enters the follicular fluid is not known, and because the granulosa cells surrounding the follicular fluid form an avascular organ, the mode of entrance of radiosulphate into the fluid is unclear. The question arises whether the granulosa cells take part in the transport of the radiosulphate to the follicular fluid, or whether their accumulation of S^{35} is merely a secondary phenomenon. Guided by the work of LEBLOND and GROSS (1948) on the mechanism of the incorporation of radioiodine in the thyroid, we have made a time-picture relation study on the uptake of radiosulphate in the Graafian follicles in the rabbit.

Experimental

27 adult female rabbits, weighing on an average 2.9 kg, were given carrier-free S^{35}-labelled sodium sulphate (obtained from A. E. R. E., Harwell, England) intravenously, in doses of 0.65 mC per kg of body

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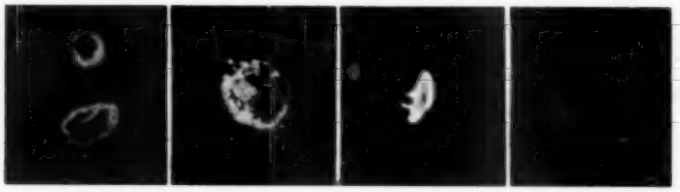
weight. Care was taken to avoid the formation of colloidal particles of radiosulphate in the solution to be injected. The animals were divided into nine groups with three animals in each, and were sacrificed 2, 4,



A. B. C. D.

Fig. 1. Typical autoradiographs of ovaries; A 2 hours, B 16 hours, C 48 hours and D 384 hours after injection. In A, small amounts of S^{35} in the theca and the granulosa and hardly any in the liquor. In B, maximum amounts of S^{35} in the theca and the granulosa, but the liquor still contains only a moderate amount. In C, the contents of S^{35} in the theca and granulosa have decreased and the liquor shows maximum incorporation of S^{35}. In D, the amounts of S^{35} in the theca, granulosa and liquor are small, but still highest in the liquor.

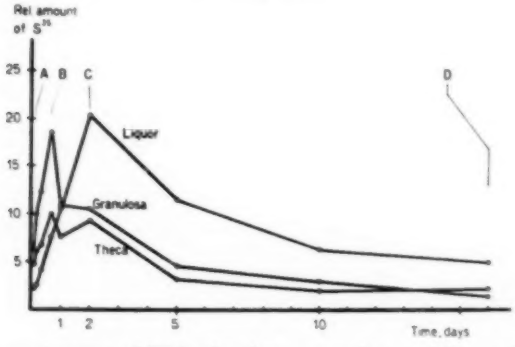


Diagram. Amount of S^{35} in the theca, granulosa and liquor folliculi at different intervals after injection.

8, 16, 24, 48, 120, 240 and 384 hours, respectively, after injection of the radiosulphate.

The animals were sacrificed by air embolism; the abdomen was opened and the ovaries removed and immediately placed for fixation in pure methanol for 24 hours. The material was then embedded in paraffin in the usual way, and cut into 10 μ thick sections, which were mounted on methacrylate slides. After deparaffination in xylene and ethanol, the

slides were pressed against a Gevaert Dentus Rapid film for exposure from 24 to 57 days. Development was then undertaken in Kodak DK 20 with KBr added to 0.2 per cent for 30 minutes at 18.3° C. After fixing, drying and removal of the fog silver on the reverse side, the autoradiographs were ready for examination. The resolution was 15 to 20 μ. The sections were stained according to Ladewig's technique and compared with the autoradiographs. Four autoradiographs from each animal were studied.

The density of the autoradiographs was assessed by *subjective estimation*. The mean error in such a single estimation is about ± 25 per cent as has been shown elsewhere (ODEBLAD 1952, II).

Results

The Graafian follicles presented a picture of greatly varying density in the different bodies. It was notable, however, that the density of both the theca and the granulosa follicular fluid reached a maximum already 16 hours after the injection of radiosulphate and that the peak of density in the follicular fluid occurred 48 hours after injection, as shown in Fig. 1 and the diagram. The amount of S^{35} in the follicular fluid was reduced to half its maximal value in about one week.

Discussion

The present study is based on the experiments of LEBLOND and GROSS (1948). These authors demonstrated the accumulation of I^{131} in the thyroid epithelium before it entered into the follicular colloid, and expressed the opinion that a synthesis of thyroid hormone takes place in the epithelium before any deposition occurs in the colloid. Our experiments support the view that a similar process takes place in the ovarian follicles, and indicate that the radiosulphate is rapidly incorporated in the granulosa cells and is then taken up by the follicular fluid. It is thus possible that there exists an intracellular mechanism in the granulosa cells, which enables the sulphate to enter the follicular fluid. The work of ODEBLAD (1952, I) as well as the results reported here substantiate the supposition that radiosulphate is incorporated in an organic compound.

SUMMARY

Radioactive sulphate was injected into rabbits, which were sacrificed 2, 4, 8, 16, 24, 48, 120, 240 and 384 hours, respectively, after injection. Autoradiographs were prepared from the ovaries, and the amount of radioactive sulphur in the theca, the granulosa and the liquor folliculi was estimated. It was found that a peak was reached

n the theca and the granulosa 16 hours after injection and in the follicular fluid 48 hours after injection. The results speak in favour of the opinion that the radiosulphate is taken up by the granulosa cells, where it may be incorporated in an organic compound of the mucopolysaccharide type before it is secreted in the follicular fluid.

ZUSAMMENFASSUNG

Kaninchen wurde radioaktiver Schwefel injiziert; die Tiere wurden 2, 4, 8, 16, 24, 48, 120, 240 und 384 Stunden nach der Injektion getötet. Von den Ovarien wurden Autoradiogramme angefertigt und der Gehalt an radioaktivem Schwefel in der Theca, der Granulosa und dem Liquor folliculi bestimmt. In der Theca und in der Granulosa konnte die Hauptmenge 16 Stunden nach der Injektion nachgewiesen werden, im Liquor folliculi erst 48 Stunden nach der Injektion.

Die Ergebnisse sprechen für die Annahme, dass der radioaktive Schwefel vor der Sekretion in die Follikelflüssigkeit von den Granulosazellen aufgenommen und in eine organische mukopolysaccharidartige Verbindung eingebaut wird.

RÉSUMÉ

Un sulfate radioactif fut injecté à des lapines qui furent sacrifiées respectivement 2, 4, 8, 16, 24, 48, 120, 240 et 384 heures après l'injection. Des autoradiographies des ovaires permirent d'évaluer la teneur en soufre radioactif de la thèque, de la granulosa et du liquide folliculaire. On constata que l'absorption du soufre radioactif atteint son maximum dans la thèque et dans la granulosa 16 heures après l'injection et dans le liquide folliculaire 48 heures après l'injection.

Ces résultats viennent à l'appui de l'opinion que le radiosulfate est absorbé par les cellules de la granulosa où il peut s'incorporer à un composé organique du type mucopolysaccharide avant d'être sécrété dans le liquide folliculaire.

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THE PROGNOSTIC IMPORTANCE OF THE GROSS MORPHOLOGY OF CARCINOMA OF THE UTERINE CERVIX

by

Ulf Borell

The prognosis of patients with carcinoma of the uterine cervix has been extensively investigated along various lines. The microscopic appearance of the growths has been carefully studied and special attention paid to the types of cell present. Many workers, however, disputed the prognostic value of grouping squamous cell carcinomata by the different types of cell found, because they failed to establish a relationship between the histologic type of carcinoma and the therapeutical results (CHAMBERS, 1935; MORTON, 1944; LAX, 1947, and others).

The clinical extent of the lesion proved to be a much better guide to the prognosis in these cases. It was observed clinically, however, that small growths, confined to the portio, grew rapidly despite adequate radiologic treatment, while extensive tumours disappeared after treatment and did not recur. The radiosensitivity of cervical carcinomata, which, microscopically, appear to be identical in type and, clinically, of the same size, may vary greatly. The difference in radiosensitivity between these tumours suggests that they also differ in other biologic characteristics.

The variations which the gross morphology of cervical carcinomata show, support this view. In contrast to the radiosensitivity, the gross morphology of the lesions may be determined objectively before treatment is begun. For this reason their macroscopic characteristics may be of value in determining the prognosis in the individual case. I was, therefore, interested in investigating the prognosis which different macroscopic varieties of carcinoma of the uterine cervix carry. Furthermore, I investigated the incidence, the length of the history in the individual case, and the frequency of the lesions in different age groups.

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The Gross Morphology of Carcinomata of the Uterine Cervix

Carcinomata of the uterine cervix have for a long time been classified by the gross morphology of the local tumour into two groups, viz. *exophytic*, *i. e.* tumours that grow outwards into the vagina, and *endophytic*, *i. e.* tumours that grow inwards and invade the deeper tissues (SCHOTTMÜLLER and KERMAUNER, 1912; KIMBROUGH and NORRIS, 1927; HOFMANN, 1939; RUNGE and WIMHÖFER, 1949; RANDALL et al., 1950; DI PALMA, 1950, and others.) However, the classification of the crateriform carcinoma, which is a very common type, presents some difficulty because it may be either endophytic or exophytic in origin. This led several workers to extend this classification to include a third group in which they placed this type (MALIPHANT, 1939; ARNESON, 1947; NOLAN, 1948, and others).

The cases of the series were also divided into three groups, viz.

1. Cases of *exophytic* or *everting* tumour. This type is usually a cauliflower growth. It may be very large and fill the entire vagina; clinically, it is often soft to the touch; miscroscopically, it contains very little connective tissue but is very vascular.

2. Cases of *endophytic* or *inverting* tumour. This tumour grows in the form of a disc beneath the cervical mucosa. Ulceration does usually not occur until late in the development of the growth, and generally involves only small portions of the surface of the growth. The surface is either even or nodular. The tumour is often very hard to the touch, probably because it contains much connective tissue and only a few blood vessels.

3. Cases of *crateriform* carcinoma. As already mentioned, this type may arise from a tumour primarily either exophytic or endophytic.

ARNESON (1947) reported that it was the everting tumour which most frequently showed a crater-like cavity because it was particularly susceptible to infection. He believed that the cancerous tissue degenerated and crumbled if a cauliflower growth became infected, resulting in the formation of a crater-like cavity. There is also the possibility, however, that a crater-like cavity is formed primarily as a result of ulceration which initially involves only the surface of the growth and does not invade the deeper tissues until much later.

Cases Studied

This investigation is concerned with the analysis of 2,794 cases of carcinoma of the uterine cervix which were referred to Radiumhemmet with a view to treatment in the years from 1914 up to and including 1941.

The total number of patients with cervical carcinoma admitted to Radiumhemmet during that period of time was 4,611; in 4,392 of these cases the patient received radiologic treatment. All case records were carefully studied. Only those cases were included, in which the gross morphology of the growth as described in the records permitted its classification by the method used. The records of many of the cases contained diagrams of coronal and sagittal sections of the true pelvis, which illustrated the extent of the growth and were very helpful in classifying them.

As already mentioned, the principle object of this investigation was to discover whether tumours, which differ in their way of growing, also differ in other characteristics. It was therefore essential that the cases studied were sufficiently well defined macroscopically to permit being correctly classified into one of the three groups mentioned. For this reason cases of endocervical carcinoma, small ulcers of the portio and cervical polypi containing cancer cells were excluded. Cases in which several conditions characterizing the three varieties of cervical carcinoma mentioned, occurred together in the same tumour, were also omitted. In 2,930 cases it was clear from the records that the carcinoma was a cauliflower growth, disc-shaped or crateriform. In 136 cases, however, a crater-like cavity was found in a cauliflower growth or disc-shaped lesion. These cases were also omitted because they did not fit into one individual group but each would have had to be placed into two of the three groups of the classification used. There thus remained 2,794 cases to be studied.

According to the pathologic reports, a squamous cell carcinoma was found in 87.1 per cent of the cases of cauliflower growth, in 84.2 per cent of the cases of disc-shaped and in 84.2 per cent of the cases of crateriform carcinoma. Hence, the distribution of squamous cell carcinoma was practically the same in the three tumour groups.

In the majority of the cases of the series the patient was examined and the extent and the appearance of the growth fully described by Professor J. HEYMAN, the risk of individual variations in interpretation thus being practically eliminated. Otherwise, it would not have been possible to use the cases for the investigation.

Method of Treatment

The patients were treated by radium combined with roentgen irradiation according to the Stockholm method. This method has been fully described in the literature (FORSSELL, 1912, 1914; HEYMAN, 1918, 1935, 1947; KOTTMEIER, 1950), and need not be discussed here. The technique employed was made to conform to the requirements of the individual case (HEYMAN, 1935, 1947; KOTTMEIER, 1950).

Results

Incidence. The incidence of cauliflower carcinoma was much lower than that of the disc-shaped and crateriform types respectively, being found only in 396 or 14.1 per cent of the 2,794 cases of this series (Table 1). The incidence of disc-shaped and crateriform carcinomata was 39.2 per cent and 46.7 per cent respectively.

Table 1

Types of case studied

Type of tumour	Number	%
Cauliflower	396	14.1
Disc-shaped	1094	39.2
Crateriform	1304	46.7
Total number of cases	2794	100.0

The figures for the incidence of these three varieties of carcinoma given in the literature vary greatly. This is probably due to individual variations in defining the growths.

SCHOTTLÄNDER and KERMAUNER (1912) were the first to investigate the incidence of exophytic and endophytic tumours; they studied 123 cases of carcinoma of the uterine cervix and reported it to be 5.8 and 94.2 per cent respectively. HOFMANN (1939), in a study of 346 such cases, found that the tumour grew outwards into the vagina in 26.9 per cent of the cases while in the remainder there was an inverting tumour. LAUTERWEIN (1947), in reviewing the cases of cervical carcinoma — 1,071 cases in all — seen at Stoeckel's Clinic in Berlin in the years 1933—1937, found the incidence of cauliflower growth to be 23.9 per cent. TRUELSON (1949), who investigated 2,918 cases of cervical carcinoma, reported that a typical cauliflower growth was present in 11.7 per cent.

As already mentioned, exophytic tumours were found in 14.1 per cent of the cases of this series while the combined incidence of the other two varieties of carcinoma which resembled endophytic tumours in type, was 85.9 per cent. These figures, however, cannot be safely compared with those given in earlier publications, because they refer to selected cases. Nevertheless, they are in close agreement with them.

The percentage distribution of the three types of tumour during different periods in the years from 1914 to 1941 is interesting to note (Diagram 1).

The curves in this graph were based on so-called 5-year moving averages consecutively covering the years 1914—1918, 1915—1919, 1916—1920,

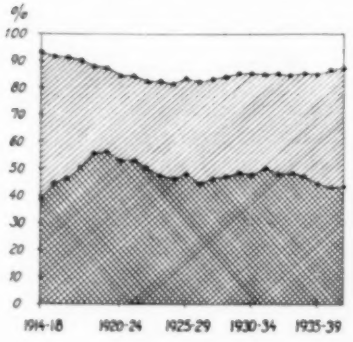

Diagram 1.

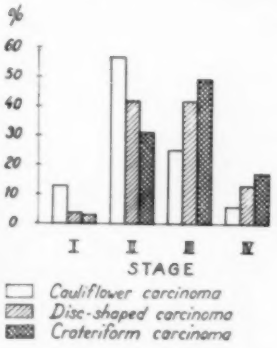

Diagram 2.

Diagram 1. Proportion of cases of cauliflower, disc-shaped and crateriform carcinoma in different 5-year periods during the years 1914—1941. The curves are based on what are known as 5-year moving averages.

Diagram 2. Distribution of cases of cauliflower, disc-shaped and crateriform carcinoma in the four stage groups.

etc. Diagram 1 shows that the percentage distribution of the three varieties was practically the same during the periods investigated. During the first years the incidence of disc-shaped carcinoma was slightly higher than that of crateriform and of cauliflower carcinoma. However the number of cases seen during those years was relatively small. For this reason the percentages should be considered with some reserve.

Stage-grouping. The cases were grouped into four stages according to the stipulations laid down by the League of Nations' Health Organisation. This classification was introduced in 1929 and was slightly modified in 1937 (Annual Report on the Results of Radiotherapy in Cancer of the Uterine Cervix, (1941); Geneva, League of Nations' Health Organisation).

Table 2

Distribution of Cases of Cauliflower, Disc-shaped and Crateriform Carcinoma in the Four Stages

Type of tumour	Stage I		Stage II		Stage III		Stage IV	
	Number	%	Number	%	Number	%	Number	%
Cauliflower	51	12.8	223	56.4	99	25.0	23	5.8
Disc-shaped	36	3.3	460	42.0	456	41.7	142	13.0
Crateriform	39	3.0	402	30.9	641	49.1	222	17.0
Total number of cases ...	126	4.5	1,085	38.9	1,196	42.8	387	13.8
Cases excluded	292	18.3	651	40.7	324	20.3	331	20.7

According to this classification cases of carcinoma of the uterine cervix are divided into four well-defined stages. Before 1929, the cases were defined as operable, borderline, and inoperable. All these cases were later re-classified using the above method of classification.

The percentage incidence of cauliflower growth in the cases diagnosed as being in Stages I and II was much higher than that of disc-shaped and of crateriform carcinomata (Table 2 and Diagram 2).

In the cases diagnosed as being in Stages III and IV the reverse was true. Although the total number of cases of cauliflower carcinoma was only one third of that of cases of disc-shaped and of crateriform tumours the absolute number among the cases in Stage I was larger than that of the other two varieties; among these early cases were 51 cases of cauliflower growth as compared to 36 cases of disc-shaped carcinoma, and 39 cases of crateriform carcinoma.

The literature gives little information about the distribution of these types of tumour in the four stages. TRUELSON (1949) found that the incidence of cauliflower carcinomata in Stages I and II was practically the same as that of cauliflower growths in Stages III and IV while the crateriform type was more frequently encountered in Stages III and IV.

As already mentioned, 1,598 cases treated in the years from 1914 to 1941 were excluded because they could not safely be referred to one of the three groups mentioned. I was interested in comparing the distribution of these cases in the four stages with the distribution of the 2,794 cases included in this investigation. The percentage incidence of cervical carcinoma in Stage I was 18.3 per cent in the former series as compared with 4.5 per cent in the latter. As already mentioned, in many of the cases excluded the growth was in an early stage and not then clearly defined, macroscopically. This might explain the striking difference in the percentage incidence of cervical carcinoma in Stage I between these two series of cases. Among the cases which were excluded, the number of patients with a carcinoma in Stage III was very small. This is difficult to explain. The percentage incidence of carcinomata in Stages II and IV was practically the same in the two series.

According to the "Annual Report on the Results of Radiotherapy in Carcinoma of the Uterine Cervix" (1951) the clinical quality of cases of carcinoma of the uterine cervix seen at the Radiumhemmet, has been modified in the course of time. The percentage number of cases in Stage II has been steadily increasing while that of cases in a more advanced stage has decreased. I was interested in investigating whether this applied equally to each of the three varieties of cervical carcinoma under discussion.

Diagram 3 (A, B, and C) shows that the percentage number of cases of cauliflower, disc-shaped or crateriform carcinoma in Stage I has remained

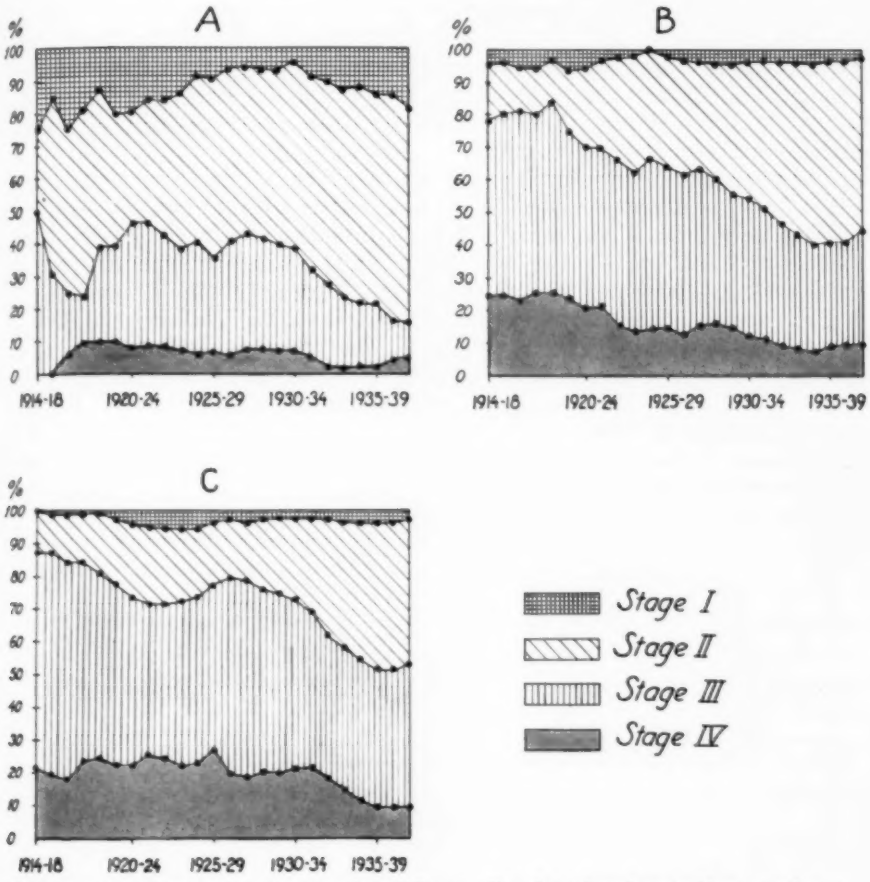

Diagram 3. Distribution of cases of cauliflower, disc-shaped and crateriform carcinoma in the four stage groups in different 5-year periods during the years 1914—1941. The curves are based on what are known as 5-year moving averages.

A Cauliflower carcinoma. B Disc-shaped carcinoma. C Crateriform carcinoma.

practically unchanged while that of cases in Stage II has steadily increased. This applied in particular to the number of patients with a disc-shaped carcinoma in Stage II. The percentage number of patients with a carcinoma in Stage III has been gradually decreasing while the fall in the percentage number of patients with a lesion in Stage IV has been less marked. This change in the proportion of the number of cases in the

different stage-groups, notably that in the proportion of the number of cases in Stage II and III, cannot solely be due to the modification of the definition of these stages as suggested by the Advisory Committee for the League of Nations Annual Report on the Results of Radiotherapy in Cancer of the Uterus, and which was adopted in Radiumhemmet in about 1935.

Diagram 3 shows that a cauliflower carcinoma in an advanced stage was found in about 15 per cent of the cases seen in the last years of the period investigated, the corresponding percentage being about 40 in the first decade of this period. The incidence of crateriform carcinoma during these two periods of time was 50 and 80 per cent respectively while that of disc-shaped carcinoma was 40 and 80 per cent respectively. The fall in the number of cases in an advanced stage has probably played a part in the rise of the 5-year apparent recovery rate which was observed at Radiumhemmet from the early 1930's onwards. There is little doubt, however, that additional factors must have been operative because the percentage 5-year apparent recovery rates for each of the four stages has been steadily increasing (HEYMAN, 1949).

Table 3

Incidence of Cauliflower, Disc-Shaped, and Crateriform Carcinomata in various Age-Groups

Type of tumour	Age										Total number of cases
	< 30 years		30—39 years		40—49 years		50—60 years		> 60 years		
	Number	%	Number	%	Number	%	Number	%	Number	%	
Cauliflower	21	5.3	96	24.2	151	38.2	75	18.9	53	13.4	396
Disc-shaped ...	29	2.6	202	18.5	354	32.4	321	29.3	188	17.2	1,094
Crateriform ...	20	1.5	165	12.7	396	30.4	409	31.3	314	24.1	1,304

Age-incidence. The incidence of carcinoma of the uterine cervix in patients of different ages has been investigated by many workers. In large series of cases the highest incidence was noted in patients of 40 to 55 years (LAUTERWEIN, 1947; INGELMAN-SUNDBERG, 1947; TRUELSON, 1949; MALIPHANT, 1949; RANDALL and collaborators 1950; MORRIS and MEIGS, 1950; DI PALMA, 1950; LINDELL, 1952, and others).

In this investigation the patients were grouped by age as recorded at the first examination at Radiumhemmet (Table 3).

The incidence of cauliflower carcinoma was highest among patients of 40 to 49 years. The incidence of disc-shaped and crateriform carcinomata was practically the same in the two decades 40 to 60.

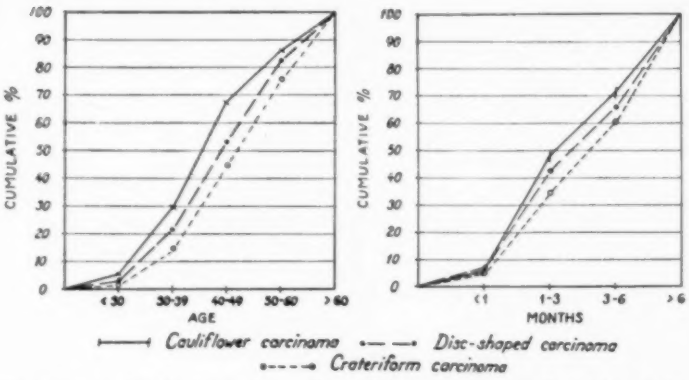

Diagram 4. Incidence of cauliflower, disc-shaped and crateriform carcinomata in different age groups.

Diagram 5. Length of the history in cases of cauliflower, disc-shaped and crateriform carcinoma.

Diagram 4 shows that a cauliflower carcinoma occurred mostly in young women while the crateriform type was commonest among elderly women. A cauliflower carcinoma was found in every third patient under 30 years and in every eleventh patient over 50 years.

Parity. Several investigations have shown that parity favours the development of carcinoma of the uterine cervix. The number of nulliparous women varied greatly in the different series of cases published, though the proportion was generally less than 10 per cent. This figure, however, refers to relatively small series of cases. In the few large series investigated this percentage was higher. BOWING (1940), RANDALL et al. (1950), BUSCH (1934) and MORRIS and MEIGS (1950) found it to be 10, 10.9, 13 and 16 per cent respectively. These figures, however, are lower than those which census returns usually show.

The incidence of nulliparous women was 14.6 per cent in this series, the distribution in the three tumour groups being practically the same (Table 4).

Table 4

Parity in Cases of Cauliflower, Disc-Shaped and Crateriform Carcinoma

Type of tumour	Number of deliveries					
	0		1—2		> 2	
	Number	%	Number	%	Number	%
Cauliflower	57	14.4	172	42.4	167	42.4
Disc-shaped	170	15.6	374	34.2	550	50.2
Crateriform	180	13.8	388	29.7	736	56.5
Total number of cases	407	14.6	934	33.4	1,453	52.0

On the other hand, the figures in Table 4 suggest that patients with a disc-shaped or crateriform lesion, notably the latter, have usually had more than two deliveries.

Length of history. It is generally believed that a cauliflower carcinoma produces symptoms earlier than a disc-shaped or crateriform carcinoma because it is very vascular and therefore tends to give rise to haemorrhage (HOFMANN, 1939; MALIPHANT, 1947; ARNESON, 1947; DI PALMA, 1950, and others). According to MORRIS and MEIGS (1950) a cauliflower growth is found in more than 50 per cent of cases with a history of symptoms of less than three months' duration while an inverting ulcerating tumour occurs twice as often in cases in which the length of the history is more than twelve months.

The length of time between the appearance of the first symptoms and the patient's admission to Radiumhemmet was also recorded in this series. Admittedly, such information is often unreliable. Nevertheless, if the series of cases investigated is large enough it is possible to gain an idea of the lenght of the history from the figures obtained.

Table 5

Length of History in Cases of Cauliflower, Disc-Shaped and Crateriform Carcinoma

Type of tumour	Length of history							
	< 1 month		1—3 months		3—6 months		> 6 months	
	Number	%	Number	%	Number	%	Number	%
Cauliflower	22	5.6	166	41.9	94	23.7	114	28.8
Disc-shaped	69	6.3	392	35.8	255	23.3	378	34.6
Crateriform	62	4.8	388	29.7	333	25.5	521	40.0
Total number of cases	153	5.5	946	33.8	682	24.4	1,013	36.3

Table 5 shows that the length of the history was more than six months in 29 per cent of the cases of cauliflower carcinoma, in 35 per cent of the cases of disc-shaped growth, and in 40 per cent of the cases of crateriform carcinoma. It was shorter than one month in about 5—6 per cent of the cases of each of these three groups. In 41.9 per cent of the cases of cauliflower growth, and in 29.7 per cent of the cases of crateriform carcinoma the length of the history varied between 1 and 3 months.

Diagram 5 and Table 5 suggest that in cases of exophytic tumour the duration of the symptoms tends to be shorter than in cases of disc-shaped and of crateriform carcinoma. The results of this investigation do not support the generally accepted view that the duration of symptoms is short in most cases of cauliflower growth. Also, there was no noteworthy

difference in the length of the history between cases in the different stages (Table 6).

Table 6

Length of the History in the Four Stage-Groups in Cases of Cauliflower, Disc-Shaped and Crateriform Carcinoma.

Stage	Type of tumour	Length of history							
		1 month		1—3 months		3—6 months		6 months	
		Number	%	Number	%	Number	%	Number	%
I	Cauliflower	2	3.9	24	47.0	14	27.5	11	21.6
»	Disc-shaped	3	8.3	12	33.4	8	22.2	13	36.1
»	Crateriform	6	15.4	11	28.2	11	28.2	11	28.2
II	Cauliflower	14	6.3	99	44.4	49	22.0	61	27.3
»	Disc-shaped	33	7.2	179	38.9	98	21.3	150	32.6
»	Crateriform	18	4.5	135	33.6	107	26.6	142	35.3
III	Cauliflower	3	3.0	34	34.0	30	30.0	33	33.0
»	Disc-shaped	32	7.0	158	34.6	109	23.9	157	34.5
»	Crateriform	32	5.0	188	29.3	165	25.7	256	40.0
IV	Cauliflower	3	13.6	9	40.9	1	4.6	9	40.9
»	Disc-shaped	1	0.7	43	30.3	40	28.2	58	40.8
»	Crateriform	6	2.7	54	24.3	50	22.5	112	50.5

However, the number of cases investigated, notably that of cases in Stage I, was very small. For this reason the figures should be considered with some reserve.

It has not yet been conclusively proved that there is a correlation between the length of the history and the clinical extent of the lesion (MALIPHANT, 1947, and others). Observations made in large series of cases of cervical carcinoma, however, suggest that patients with a carcinoma in an advanced stage usually have had symptoms for quite a long period before seeking medical advice while in the cases, in which the lesion was in a relatively early stage, the duration of symptoms was usually short (van ECK-VERMANDE and WASSINK, 1946; JACOBY, 1947; KAHANPÄÄ and KANKKUNEN, 1949). In this investigation the highest percentage of cases (40 per cent), in which the length of the history was more than 6 months, was found among patients with a tumour in an advanced stage (Table 6). On the other hand, the view that the duration of symptoms is usually shorter than three months in cases of cervical carcinoma in an early stage was not borne out in this investigation.

It is interesting to note that in three cases of cauliflower carcinoma in Stage IV it was noted in the records that the patient had had symptoms for less than one month. According to the literature this type of carcinoma

usually produces symptoms early. The three cases just discussed show that it may also happen that this growth does not give rise to symptoms until late in its development. This was also pointed out, among others, by RUNGE (1940).

Prognosis. According to several workers, cases of exophytic tumour carry a better prognosis than do cases of endophytic tumour. Several explanations have been offered for this observation. Some workers feel that the marked radiosensitivity of exophytic tumours is an important factor (ADLER, 1947; ARNESON, 1947). Others again, express the view that this type of tumour remains confined to the cervix for quite a long time and does not invade the deeper tissues and adjacent areas until

Table 7

5-year Apparent Recovery Rate in Cases of Cauliflower, Disc-Shaped and Crateriform Carcinoma

Type of tumour	Total number of cases	Apparently recovered at end of 5 years. Number of cases	%
Cauliflower	396	157	39.7
Disc-shaped	1,094	299	27.3
Crateriform	1,304	311	23.8

fairly late (NOLAN, 1948; RANDALL and collaborators, 1950). It has also been suggested that the comparatively favourable prognosis of patients with an exophytic tumour is due to the fact that they soon experience symptoms and therefore seek medical advice early (MALIPHANT, 1947; DI PALMA, 1950).

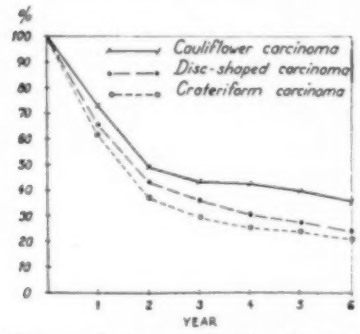

Diagram 6. Curves showing the percentages of patients surviving in different years after treatment.

LAUTERWEIN (1947) reported that the percentage 5-year apparent recovery rate for cauliflower and crateriform carcinomata was 32.8 and 16.5 per cent respectively. He did not investigate however, the percentage distribution of the apparent 5-year recovery rate in the four stage groups. HOFMANN (1933), in a study of the prognosis which different macroscopic and microscopic types of carcinoma of the uterine cervix carry, investigated 346 cases which were grouped by Schmitz' classification. He found that the prognosis of patients with an exo-

phytic carcinoma in Stage I, II or III was slightly better than that of patients with an endophytic growth in these stages. A close study of the percentages given by this author revealed that the difference in prognosis between these two types of carcinoma was greatest in the cases in which the growth was in Stage II. The cases of endophytic tumour of his series, which showed a deep craterlike cavity, carried the worst prognosis. However, it is not possible to draw any definite conclusions from the figures given by HOFMANN because the number of cases which he investigated was too small.

Table 7 shows the 5-year apparent recovery rates in this series. They are expressed as a percentage of the total number of cases in the individual tumour groups. The prognosis of the patients with a cauliflower growth was better than that of patients with a disc-shaped or crateriform carcinoma, the 5-year apparent recovery rate being 39.7 per cent. In the cases of disc-shaped and crateriform carcinoma the corresponding percentage was 27.3 and 23.8 per cent respectively.

The number of patients surviving in each successive year after radiologic treatment is interesting to note. Diagram 6 shows that the prognosis of patients with an exophytic tumour was better than that of patients with a crateriform lesion, particularly during the first years after treatment during which the latter cases carried a bad prognosis.

On analysing the cases of each stage group separately it was found that the prognosis of patients with a cauliflower, disc-shaped or crateriform carcinoma in Stage I was practically the same (Diagram 7).

The late prognosis of patients with a cauliflower growth in Stage II, however, was better. The number of patients with such a tumour who died in the first two years following radiologic treatment, was practically the same, irrespective of the macroscopic type of tumour present. It was not until the third year after treatment that it became apparent that the prognosis of these patients was better than that of patients with a disc-shaped or crateriform lesion. There was no difference in the percentage survival rate in cases in which the growth was in an advanced stage, irrespective of the macroscopic type of tumour present.

I also investigated the question whether any relationship exists between the age of the patient at the time of the radiologic treatment and the survival rate (Diagram 8).

The patients were divided by age into five groups, viz. three groups which included patients of 30 to 60 years, and two groups comprising patients under 30 and over 60 years respectively. In all these groups the highest percentage yearly survival rate was found among patients with a cauliflower growth. Thus the prognosis of a patient with an exophytic tumour in Stage II is better than that of a patient with a disc-shaped or

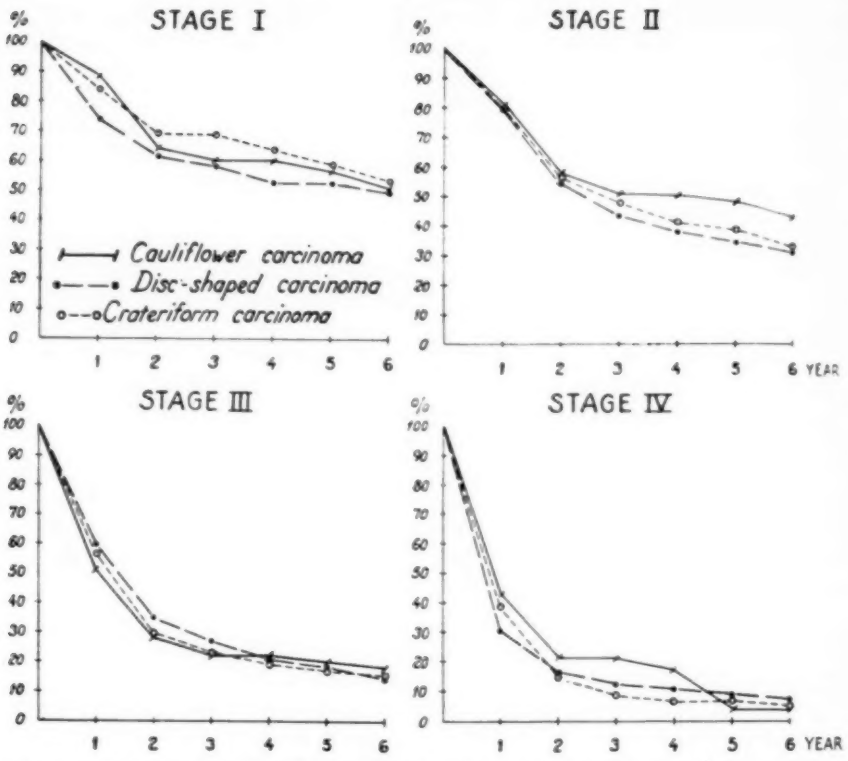

Diagram 7. Percentage distribution of patients surviving in the four stage groups in different years after treatment.

crateriform carcinoma in Stage II, irrespective of the age she receives radiologic treatment.

In cases of crateriform carcinoma the age of the patient seems to influence the prognosis. The percentage survival rate was very low in this group, notably in young patients and in those over 60.

Discussion

In an investigation into the gross morphology of carcinomata of the uterine cervix, the classification of the growth is a stumbling block and gives rise to much discussion because it is based solely on the findings on vaginal examination. Neither the classification into exophytic and endophytic tumours nor the grouping into everting, inverting and crateriform

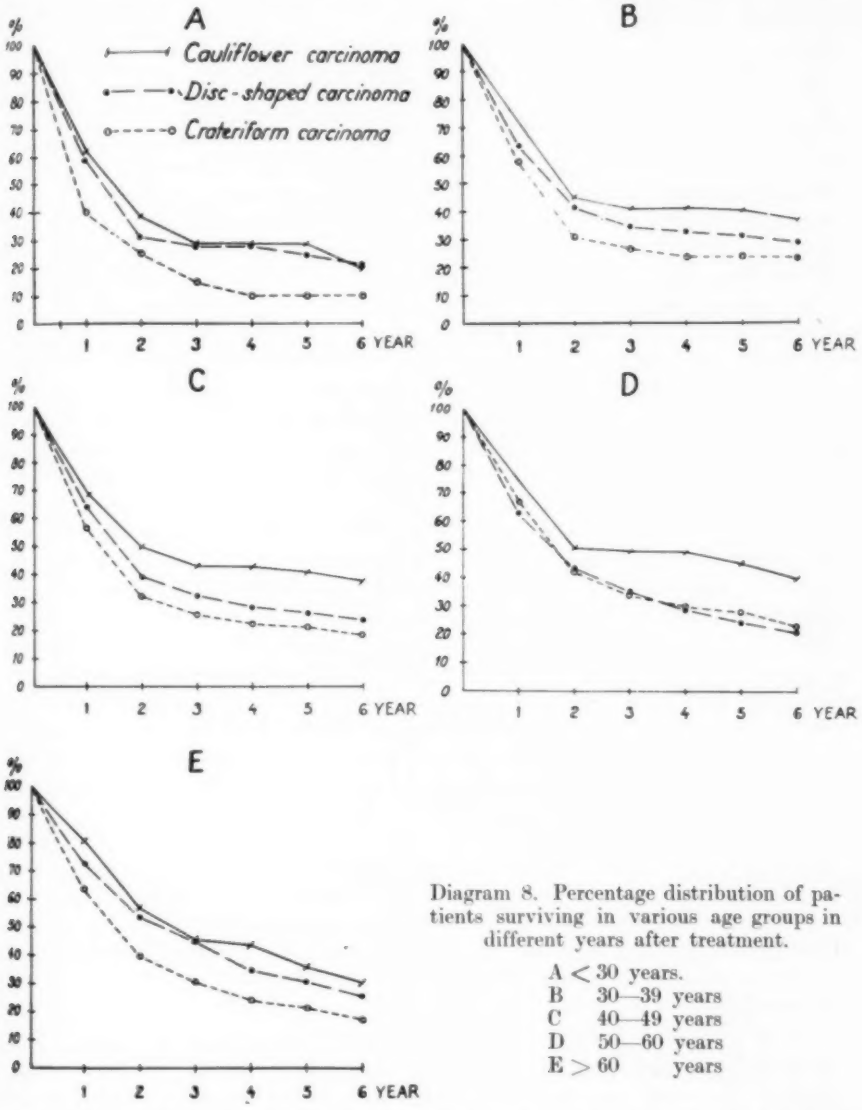

Diagram 8. Percentage distribution of patients surviving in various age groups in different years after treatment.

A < 30 years.
B 30—39 years
C 40—49 years
D 50—60 years
E > 60 years

tumours, widely used in England and America, is satisfactory, because eversion and inversion may occur at the same time in the same tumour; moreover there are transitional forms of growth which are ill-defined

macroscopically. The differential diagnosis between an ulcerating disc-shaped tumour and a crateriform lesion may present considerable difficulty. This investigation has shown also that there are cases of cervical carcinoma, in which conditions characterising the three types occur together in the same tumour.

As already mentioned, it is not possible to say whether the crater-like cavity develops primarily or whether it is produced secondarily in a carcinoma which initially was a cauliflower or disc-shaped growth. It is most frequently observed in tumours in an advanced stage. RUNGE and WIMHÖFER (1949), in a study of the prognosis and gross morphology of carcinomata of the uterine cervix, excluded cases in Stage IV because they felt that it was not possible to determine whether the tumour, in most of these cases, was initially endophytic or exophytic. In this investigation, however, such cases were taken into account, the principle reason being that the series studied included a relatively large number of cases of cauliflower and disc-shaped carcinomata in Stage IV. Hence, there seem to be a good many cases of cervical carcinoma in Stage IV, which do not show a crater-like cavity.

In the majority of the cases of cauliflower growth of this series the tumour was in an early stage when the patient was seen for the first time. In this respect this type of tumour differed from the disc-shaped and crateriform carcinomata. There are several explanations for this observation: (1) In a good many cases of exophytic tumour the patient experiences symptoms early and therefore also seeks medical advice early. However, the observations made in the cases of this series suggest that these factors do not play an important part. The length of the history was practically the same in the cases of cauliflower, disc-shaped and crateriform carcinoma. Nor was there any noteworthy difference in the length of the history between such cases in different stages. (2) The cauliflower carcinoma degenerates and crumbles as it grows which results in the formation of a craterlike cavity. Such cases, no doubt do occur, though it is difficult to determine their incidence. (3) The cauliflower carcinoma grows slowly and is clearly demarcated from the surrounding tissues. In these cases the tumour bed probably forms a barrier which is more resistant than that in cases of disc-shaped or crateriform carcinoma, in which it is easily penetrated.

The results of the investigation into the prognosis of patients with a cauliflower, disc-shaped or crateriform carcinoma of the uterine cervix support this assumption. Only the cases of exophytic carcinoma clinically in Stage II, carried a better prognosis than the cases of disc-shaped and crateriform carcinoma. On the other hand, these three types of carcinoma in Stage I, III and IV carried practically the same prognosis.

In the Stage I group the carcinoma is in most cases strictly confined to the cervix. The prognosis for the patient, therefore, is good, while in the cases in Stage III and IV, the extent of the growth is so great that the therapeutic outlook is unfavourable, irrespective of the macroscopic type of growth present. It might, therefore, be expected that the prognosis for a patient with a cervical carcinoma that has invaded the parametrium only to a lesser extent, is better. KOTTMEIER (1952), in a study of 1,440 cases of carcinoma of the uterine cervix treated at Radiumhemmet in the years 1936 to 1945, furnished evidence that this is actually true. All these cases were primarily diagnosed as being in Stage II. Later, however, they were subdivided into two groups, viz. group 1, which included cases "with no definite involvement of the paracervical or paravaginal tissue on clinical examination"; group 2, which included cases "with definite involvement of the paracervical or paravaginal tissue". The survival rate at the end of 5 years in the two groups was 64.2 and 46.0 per cent respectively. These figures illustrate clearly that the prognosis for patients with a cervical carcinoma in Stage II, which, clinically, has not spread beyond the cervix, is better than the prognosis for those with a carcinoma that has partly invaded the parametrium.

The observation that the prognosis for patients with a cauliflower growth in Stage II is relatively better than that for patients with a disc-shaped or crateriform lesion in Stage II strongly suggests that this type of carcinoma has biologic characteristics other than its manner of growth as apparent on vaginal examination and that these have a bearing on the end results. The fact that this type occurs more frequently among young than among elderly women is further evidence in support of this view. There are thus good reasons to assume that the classification of carcinomata of the uterine cervix by their gross morphology is not only theoretically interesting but may also be helpful in ascertaining the prognosis in such cases.

Conclusions

1. The investigation has shown that: Disc-shaped and crateriform carcinomata were three to four times more common than the cauliflower carcinoma.

2. In the majority of cases of exophytic cauliflower carcinoma the growth was in Stage I or II when the patient presented herself for examination while in most cases of disc-shaped and crateriform carcinoma the growth was in Stage III or IV.

3. The cauliflower carcinoma was more common among young women while disc-shaped and crateriform carcinomata occurred more frequently in older age groups.

4. The length of the history was practically the same in the cases of cauliflower, disc-shaped and crateriform carcinoma. It was suggested, however, that the interval between the appearance of the symptoms and the first examination of the patient was somewhat shorter in cases of exophytic tumour than in cases of endophytic tumour.

5. The prognosis of patients with an exophytic tumour was better than the prognosis of patients with an endophytic tumour. The difference in prognosis, however, was appreciable only in cases clinically diagnosed as being in Stage II.

SUMMARY

Between the years 1914 and 1941 inclusive, 4,611 cases of carcinoma of the uterine cervix were seen at Radiumhemmet. The records of all these cases were carefully studied, and special consideration given to the description of the gross appearance of the growths. In 2,794 of these cases the growths were macroscopically well defined which made it possible to classify them into three groups: (1) exophytic cauliflower carcinomata, (2) disc-shaped carcinomata and (3) crateriform carcinomata.

There are good reasons to assume that the classification of carcinomata of the uterine cervix by their gross morphology may be of value in ascertaining the prognosis.

ZUSAMMENFASSUNG

Während der Jahre 1914 bis einschl. 1941 kamen 4,611 Fälle mit Carcinoma cervicis uteri im Radiumhemmet zur Untersuchung. Die Krankenblätter aller dieser Fälle wurden sorgfältig studiert und besondere Aufmerksamkeit wurde der Beschreibung des makroskopischen Aussehens der Geschwülste gewidmet. In 2,794 Fällen waren die Geschwülste makroskopisch gut definiert; hierdurch war es möglich, sie in 3 Gruppen einzuteilen: 1. Exophytische, blumenkohlartige Karzinome, 2. Diskusförmige Karzinome, 3. Kraterförmige Karzinome.

Es ist wohlberechtigt anzunehmen, dass die Einteilung des Carcinoma cervicis uteri auf der Basis der makroskopischen Morphologie für die Beurteilung der Prognose wertvoll sein möge.

RÉSUMÉ

De 1914 à 1941 inclusivement 4,611 cas de cancer du col de l'utérus ont été vus au Radiumhemmet. Les observations de tous ces cas ont été soigneusement étudiées et la description de l'aspect macroscopique des tumeurs a été l'objet d'une attention particulière. Dans 2,794 de ces cas les tumeurs étaient macroscopiquement bien définies, ce qui a permis de les classer en trois groupes: 1) cancers bourgeonnants en chou-fleur, 2) cancers nodulaires, 3) cancers ulcéreux.

Il y a de bonnes raisons d'admettre que la classification des cancers du col de l'utérus d'après leur morphologie macroscopique peut avoir de la valeur pour fixer le pronostic.

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SURVIVAL TIME IN WOMEN WITH DISSEMINATED BREAST CANCER, FOLLOWING TESTOSTERONE TREATMENT

by

O. Hallberg, B. Nohrman and *B. Sylvén*

The palliative effects of androgen treatment in women with disseminated breast cancer are poorly understood. It seems apparent that the clinical course in some cases may be retarded or accelerated by androgens as well as by estrogens (2, 3, 6, 7, 13), but if this results from general systemic influence or by direct or indirect action on cancerous foci is not clear. Since gross shrinkage of tumors or obvious cytologic evidence of tumor regression is only registered in a limited number of cases (3, 6, 7, 13), and since satisfactory methods for direct registration of cancerous growth rate are lacking, further information may be obtained by continued careful observation of patients under treatment. In this paper data are presented on the alleged influence of androgen treatment on the length of survival in women with skeletal metastases from mammary cancer. This aspect was touched upon by previous authors. According to the Subcommittee on Steroids and Cancer, no apparent increase in mean survival time was found in their androgen treated series (2). A recent statement by DOUGLAS (3) that "... it seems that life can be prolonged with hormone treatment, ..." seems mainly to refer to estrogen treated series. A similar suggestion by LEWISON and CHAMBERS was not supported by actual evidence. The complexity of the problem and difficulties inherent in the statistic treatment of the material were recently stressed by NATHANSON (7). It is clear that a statistic approach alone will not answer questions relating to the operating mechanisms of androgenic response.

Submitted for publication, Sept. 17, 1952.

This paper contains a statistic analysis of length of survival in a series of women with skeletal carcinosis receiving androgen treatment from the end of 1947 until April 1952. Part of the present series was included in a previous report. All cases presenting unequivocal signs of visceral involvement at the time of onset of bone metastases have been excluded, because our results with androgen treatment in those cases have largely been disappointing (13), and, further, our present inability to estimate the extent of visceral deposits. The significance of this limitation of material will be discussed below (cf. also 13, p. 410). The test series is compared with a similar control material carefully scrutinized in order to justify the use of statistics.

Material and Methods

Control Series. — Our control series comprises a total number of 254 verified cases of mammary cancer with skeletal carcinosis seen at the hospital from 1936 to the end of 1946. All cases with skeletal involvement are included irrespective of the presence of axillar and/or supraclavicular lymph nodes at the onset of bone metastases; but all cases with obvious signs of visceral involvement at the time when skeletal spread was diagnosed have been excluded. This means that those patients were excluded who had evidence of skeletal foci at a time when already a short survival could be expected due to extensive internal spread. Most of the control patients received palliative roentgen treatment to the bone lesions when necessary. At the onset of skeletal spread, 92 patients were in the child-bearing ages, and out of these 49 underwent castration by irradiation. Arrest of cancerous growth and an increased survival rate following castration by irradiation as claimed by previous authors (1, 14, 15) was not verified in this material, and therefore all fertile women in this group were included as controls irrespective of castration. The control series was divided in two sub-groups, viz. patients of child-bearing ages, and those of post-menopausal ages, and comparison will be made with the corresponding sub-groups of the test material (Tables 1—3). We consider the control material to be comparable with the test material, but realize that conclusive evidence to this effect seldom can be presented.

Test Series. — Long-term androgen treatment was given to 97 women with disseminated skeletal spread of mammary carcinoma following radical mastectomy and postoperative roentgen treatment. In this group, 57 cases were post-menopausal and 40 belonged to the child-bearing ages. Of the latter, all but 4 patients had previously undergone castration by irradiation. The ratio between the number of pre- and post-menopausal women was thus different in this series from that in the control series, which is of significance. All cases continuously received intramuscular injections of testosterone propionate according to our previously described dosage regimen (13) until they succumbed. The average dose was 225 mg per week until subjective response, and then continuously 150 mg weekly as a maintenance dose. The total doses ranges are given in Table 4.

Statistic Evaluation of Survival. — The time of observation has in most cases been calculated from the date when skeletal spread was first diagnosed by roentgen examination. In spite of bone pain a few patients delayed visiting the hospital for six months; in these cases the observation time has been calculated from the date of onset of the pain.

The calculation of the percentage of survivals has been made by a variation of the ordinary life table method (8, 9). For each year of observation we calculated the quotient (q) between the number of cases alive at the end of the year and the number exposed to the risk of dying during the same year. Therefore for each year of observation

$$q = \frac{\text{number of survivals at the end of the year}}{\text{number of survivals at the end of the year} + \text{number of deaths during the year}};$$

and the accumulated percentage of survivals after n years is

$$100\ (q_1) \cdot (q_2) \ldots\ldots\ldots\ (q_n).$$

The usual way of calculating the percentage of survivals as 100 times the quotient between the number of survivals after n years and the number observed during n years, can only be used for a period of observation not exceeding the length of time during which the whole material has been observed. For only under such conditions will both methods of calculation give identical figures. In our material every case has been observed during at least one year, part of the material has been observed during two years, a smaller part during three years, and so on. The usual method of calculation mentioned above can thus only be applied to the results at the end of one year. Since after this period of observation the number of cases decreases each year, a method of calculation must be used which takes into consideration the number of cases every year exposed to the risk of dying, without omitting any part of the material (9).

Results and Comments

The materials are presented for comparison in Tables 1—3, and in the diagram. A significant increase in survival length is found in the total androgen treated series during the first to the end of the fourth year after the onset of skeletal metastases (see diagram). This relative increase of survival is most marked in the post-menopausal group (Table 2). In the fertile group neither radiologic castration (details omitted)

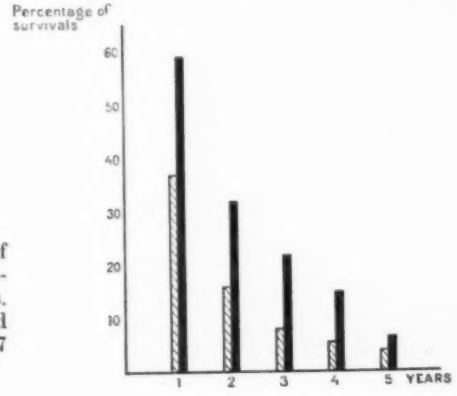

Diagram. Accumulated percentage of survivals at end of each year of observation after onset of skeletal metastases. Controls (254 cases) represented by dashed piles and androgen treated series (97 cases) by full piles.

nor castration plus testosterone treatment had any significant influence on the survival rate during the first and second years of skeletal spread (Tables 1 and 3). Apart from this it may be mentioned that about 80 to 90 per cent of our androgen treated patients showed improved general

Table 1

Survival in fertile ages

Year after onset of metastases	Control series			Androgen treated series		
	Exposed to risk of dying	Survivors at end of year	Accumul. percentage of surv. at end of year	Exposed to risk of dying	Survivors at end of year	Accumul. percentage of surv. at end of year
1	92	48	52	40	24	60
2	47	19	21	23	10	26
3	19	9	10	7	6	24
4	8	4	5	3	3	24
5	4	3	4	3	1	8

Table 2

Survival in post-menopausal women

Year after onset of metastases	Control series			Androgen treated series		
	Exposed to risk of dying	Survivors at end of year	Accumul. percentage of surv. at end of year	Exposed to risk of dying	Survivors at end of year	Accumul. percentage of surv. at end of year
1	162	46	28	57	33	58
2	44	20	13	32	20	36
3	19	10	7	16	10	23
4	10	8	6	9	5	13
5	8	7	5	4	2	6

Table 3

Mean survival times in months after onset of skeletal metastases

All cases included

	Childbearing ages	Post-menopausal ages	All cases
Control series			
254 cases	17 mths	13 mths	15 mths
Androgen treated series			
97 cases	19 mths	22 mths	21 mths

Table 4

Palliative response in androgen treated series

Group	Total number of patients	Total dosage range in mg	Number of patients with improved general condition and relief of pain		No improvement
			Marked improvement	Moderate or slight improvement	
Fertile non-castrated women ...	4	1,500—7,000	1	1	2
Fertile roentgen castrated women	36	2,000—15,900	20	11	5
Postmenopausal women	57	2,000—13,000	39	11	7
Total No.	97		60 (62 %)	23 (24 %)	14 (14 %)

well-being (Table 4). Similar striking improvement was not observed in a few debilitated cases treated with large doses of dehydroandrosterone (*Organon*) or methylandrostenediol (*Ciba*) (cf. 5, 12).

These data thus tend to indicate that continuous large doses of testosterone propionate increases the length of survival in post-menopausal mammary carcinoma patients with bone involvement during the first four years after the onset of skeletal spread; this means that a larger number of patients will survive two to four years than those devoid of androgen treatment. Similar result was, however, not found in previously castrated or non-castrated fertile women. If in addition the very marked palliative effects are considered the collection of more clinical experience with androgen as well as with other forms of endocrine treatment seems highly justified.

The frequently reported 'objective' effect of androgen treatment in the sense of increased remineralization of bone foci was discussed in a previous paper (13), but we feel this poorly defined phenomenon to be of little value for objective assessment of response so far as cancerous bone lesions are concerned. The frequency of temporary recalcification was about 30 per cent in androgen treated cases (cf. 6 and 11), but most of these patients simultaneously exhibited new osteolytic bone foci or visceral involvement. The recalcification process may be correlated to the duration of bone foci rather than to the growth rate and rate of spread of mammary cancer.

In view of the wide variations in the natural history of mammary carcinoma we present no comparison of the total duration of the disease in the androgen-treated and the control series. After the onset of the disease, the patients develop skeletal metastases at indefinite times, and the period during which palliative androgen treatment is administered is comparatively short. This may form a subject for those investigators who favour so-called 'prophylactic' androgen treatment (PRUDENTE, a. o.).

For reasons stated above, the material was limited to cases with skeletal metastases only, and the significance of this has to be discussed. Since skeletal metastases *per se* are in general of little influence on the final outcome of the disease the present manner of comparison may be doubted. We have registered the duration of life from the time of onset of bone metastases until death, irrespective of soft tissue involvement appearing during the period of observation. This was done because bone lesions are readily diagnosed and are often the first objective sign of generalized spread. Since both the control and the test patients developed skeletal involvement at indefinite times during the disease, and moreover since both materials are large enough, we believe the present statistical results to be as significant as can be expected from the clinical survival data.

In their very advanced testosterone treated series of patients with bone metastases, the Subcommittee on Steroids and Cancer (2) found approximately the same mean survival figures as in the control material published by GARLAND et al. (4); this finding was evidently deemed insignificant. Since their series under endocrine treatment was in a more advanced stage than the corresponding control material, we consider, on the other hand, that the findings of the Subcommittee may indicate a real increase in survival time, provided a comparable control material was used.

As previously suggested (13), the clinical data indicate that androgens may in most cases operate via the tumour-host relationship and not as 'carcinolytic agents'. This would explain why regressive changes in cancer foci are seldom found. On the other hand, this will not explain why androgens are not equally effective in fertile women (castrated or non-castrated) and in patients with visceral involvement.

Acknowledgements

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SUMMARY

Testosterone propionate was administered to 97 women who had developed skeletal carcinosis after radical operation for mammary cancer. Improved general condition and considerable palliation was obtained in about 85 per cent of the patients. The mean survival time of this test material was compared to that of a control series comprising 254 similar cases of skeletal carcinosis in which palliative roentgen treatment to the bone lesions had been given. The data suggest that androgen treatment significantly increases the length of survival. Thus, the mean survival time from the onset of skeletal

carcinosis was 21 months in the total androgen series, as compared with 15 months in the controls; in the post-menopausal groups the corresponding figures were 22 and 13 months, respectively. No significant increase in the survival time could be demonstrated in the fertile group of women.

ZUSAMMENFASSUNG

97 Frauen, bei denen nach Radikaloperation wegen Carcinoma mammae Knochenmetastasen zur Entwicklung kamen, wurden mit Testosteronpropionat behandelt. Verbesserten Allgemeinzustand und bedeutende Palliation erhielt man bei etwa 85 % der Patienten. Die durchschnittliche Überlebenszeit dieses Versuchsmaterials wurde mit der einer Serie von 254 ähnlichen Fällen mit Skelettmetastasen verglichen, die palliative Röntgenbehandlung der Skelettveränderungen erhalten hatten. Das Resultat deutet an, dass die Androgenbehandlung die Überlebenszeit deutlich verlängert. So ist die durchschnittliche Überlebenszeit von Beginn der Knochenkarzinose an 21 Monate in der Androgenserie und 15 Monate in der Kontrollserie; für die postmenopausalen Gruppen ergaben sich 22 bezw. 13 Monate. In der fertilen Gruppe konnte kein deutliches Ansteigen der Überlebenszeit demonstriert werden.

RÉSUMÉ

L'administration de propionate de testostérone à 97 femmes atteintes de carcinomatose du squelette après opération radicale pour cancer du sein a donné une amélioration de l'état général et un effet palliatif considérable dans environ 85 % des cas. La durée moyenne de survie de cette série fut comparée à celle d'une série témoin de 254 cas semblables de carcinomatose du squelette ayant subi un traitement roentgenthérapique palliatif de ses lésions osseuses. Les résultats font penser que le traitement par les androgènes augmente de façon significative la durée de la survie. La survie moyenne depuis le début de la carcinose osseuse fut de 21 mois dans l'ensemble de la série traitée par les androgènes, de 15 mois dans les cas témoins; dans les groupes postménopausiques les nombres correspondants étaient respectivement de 22 et 13 mois. Aucune augmentation significative de la durée de survie n'a pu être mise en évidence dans le groupe des femmes en période d'activité génitale.

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FROM THE ROENTGEN CLINIC (DIRECTOR: DR. KRISTIAN OVERGAARD), THE COUNTY AND CITY HOSPITAL, VIBORG, DENMARK

A CASE OF DUODENOHEPATIC REFLUX DEMONSTRATED BY ROUTINE BARIUM MEAL

by

Carl Erik Lampe

It is seldom that the biliary passages are filled with contrast medium in the ordinary roentgenologic examination of the stomach, and the rarity justifies the publication of such a case. In a review of the literature, BORMANN and RIGLER (1937) found 83 cases and reported 8 cases of their own. In 1942, GARLAND and BROWN collected a total of 90 cases.

Case Report

A woman, aged 70, had for 16—17 years suffered from slight dyspepsia with periodic epigastric pain and nausea. For three years previously the pain had moved to the region below the right costal margin but was not intense. Twelve months previously, the patient had been in bed at home for 4—5 weeks with cholecystitis accompanied by fever and slight jaundice. Otherwise she had had no previous illnesses and had not undergone operation.

Physical examination: Weight 54 kg, height 151 cm. Slight tenderness in the epigastrium and below the right costal margin; otherwise the examination did not reveal any abnormalities. Urine analysis showed no signs of albumin, sugar, urobilin or bile pigments.

Roentgen examination: Stomach normal; the duodenal bulb filled well without any signs of ulcer; the descending part of the duodenum was normal and presented the usual mucosal pattern. The contrast medium passed freely into the biliary passages. The common bile duct (Fig. 1), the hepatic duct and several branches of the hepatic tree were filled with contrast medium; the cystic duct and, to some extent, the gall bladder were also outlined (Fig. 2). The anatomy of the biliary passages seemed to be normal and there was no connection between them and the duodenal bulb or the stomach. In two or three films, air was seen in the biliary system.

Cholecystography: no contrast filling of the gall bladder.

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Fig. 1. The common bile duct filled with barium contrast from the descending part of duodenum.

Fig. 2. The contrast has filled the hepatic duct and its main branches as well as the cystic duct and partially the gall bladder.

The passage of barium into the biliary passages may be due to (1) a fistulous communication between the biliary passages and the gastrointestinal tract or to (2) atony of the common duct resulting in patency of the sphincter of Oddi. (A third but extremely rare cause is an abnormal course of the common duct with a termination in the duodenal bulb.)

By roentgen examination it is possible to determine to which group the abnormality belongs. The fistulous communication (Group 1) opens generally into the duodenum; in these cases the lower part of the bile duct usually is not visible, and in case of retrograde filling, this occurs slowly and is only incomplete. In Group 2 (patency of the sphincter of Oddi) normal conditions are found in the duodenum; the bile duct is visible throughout its entire length with a normal termination in the duodenum. Retrograde filling occurs rapidly and is complete (SALVATI, 1947). It may be added that the demonstration of the passage of barium into the common bile duct from the descending portion of the duodenum

under fluoroscopic control further substantiates the diagnosis of patency of the sphincter of Oddi.

Thus, in the case reported here the passage of barium must have been due to patency of the sphincter of Oddi, which is a less frequent cause than passage through a fistula; FAUST and MUDGETT (1943) found only 17 cases of this type in the literature.

Patency of the sphincter of Oddi may arise in various ways. Thus, the causes reported in the literature were as follows: GABRIEL (1933), JOHANNESON (1929) and VENABLE and BRIGGS (1921): calculi in the common bile duct; CHRISTOFANETT (1938), JOHANNESON (second case) and STEPHENSON (1921): cholecystitis; AKERLUND (1917) and BEALL and JACODA (1921): pancreatitis; FISHBAUGH (1926) and PENNINGTON (1932): pancreatic cancer; BEALL and JACODA (second case): enlarged pancreas; VENABLE and BRIGGS (second case): gastric cancer; LEVY (1935): duodenal ulcer; FAUST and MUDGETT (1943): adhesions between the gall bladder and duodenum; WICHTL (1937): scar formation at the papilla of Vater; JENKINSON and BRONZE (1931) and TITONE (1936): previous operation. SIGHINOLFI (1926), REES (1933), and BÉCLÈRE and PORCHER (1934) also described contrast filling of the biliary passages due to patency of the sphincter of Oddi. A similar case was reported by ARNTZEN (1932); however, he was not quite sure of the cause of the passage of the barium, but the roentgenograms showed conditions resembling those seen due to patency of the sphincter of Oddi.

Passage of barium through fistulous communications most frequently occurs through a fistula between the gall bladder and the duodenum (first described by BUSI in 1921). Less frequently, a fistula may be present between the common bile duct and the duodenum; furthermore, it may be mentioned that a barium enema may fill the biliary passages through a fistula between the colon and the gall bladder. The danger of cholangitis arising from barium enema examinations has been the subject of some discussion, but no cases have been described.

The fistulae may occur spontaneously (most commonly by perforation by a gall stone), or after operation. More uncommon causes are gastric cancer (reported by BEUTEL and CARMAN), pancreatic cancer, rupture of a hepatic abscess and hydatid cyst (described by AUBRY, 1927).

The symptoms as well as treatment depend on the underlying disease. Thus, the case reported by FAUST and MUDGETT became symptom-free after separation of the adhesions, but the roentgenographic appearances remained unchanged.

Finally, it may be mentioned that air as well as contrast medium may be found in the gall bladder, as in my own case and that its presence has been reported in several cases in which no contrast medium had

been used. Air in the gall bladder may be due to (1) the presence of gas-forming bacteria, (2) a fistula between the biliary passages and the gastro-intestinal tract, or (3) patency of the sphincter of Oddi. WAHLBERG (1927) found gas-forming bacteria in 4 cases out of 1,000 gall bladder operations. POWERS (1936) described 4 cases in which the presence of air in the gall bladder was attributed to fistulous communications, and FAUST and MUDGETT (1943) reported one case in which the cause was patency of the sphincter of Oddi, whereas air was not present in the biliary passages in the 17 cases they had found in the literature.

SUMMARY

A case of the passage of contrast medium into the biliary passages after its oral administration during a routine barium meal, is reported. The cause was patency of the sphincter of Oddi. The patient had had cholecystitis but had not been operated upon.

ZUSAMMENFASSUNG

Ein Fall wird berichtet, in dem Kontrastmittel nach oraler Administration einer gewöhnlichen Bariummahlzeit in die Gallenwege eindrang. Die Ursache hierfür war ein offenstehender Sphincter Oddi. Die Patientin hatte eine Cholecystitis gehabt; Operation war nicht notwendig.

RÉSUMÉ

Présentation d'un cas de passage du produit de contraste dans les voies biliaires après administration d'un repas baryté. La cause en était la béance du sphincter d'Oddi. La malade avait eu une cholécystite, mais n'avait pas été opérée.

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BOOK REVIEWS

MASS, LIPIDS, PENTOSE NUCLEOPROTEINS AND PROTEINS DETERMINED IN NERVE CELLS BY X-RAY MICRORADIOGRAPHY. By Sven-Olof Brattgård and Holger Hydén. 48 pp. 33 illustrations, 6 tables. Acta radiol. Suppl. 94, Stockholm 1952. Sw. Kr. 15:—.

The authors describe a method by which it is possible to determine the content of lipids, pentose nucleoproteins (PNP) and proteins in single nerve cells, using roentgen microradiography at 8—10 Å according to ENGSTRÖM and LINDSTRÖM. The results are expressed in terms of the dry weight per μ^3 of the cell section. The thickness of the section is determined after the cytologic treatment. The resolving power of the method lies at 4 μ^2. A modification of the roentgen microspectrograph designed by ENGSTRÖM and LINDSTRÖM is described. Data are also given for a new self-recording microphotometer and for an interferometer to measure thin cellulose foils used as a reference system.

An investigation is made of some factors of importance for the reliability of absolute values of mass obtained in roentgen microradiography of biologic tissue.

The absorption in the sample is compared with that of a reference system consisting of 0.5—5 μ thick nitrocellulose foils. The mass of the biologic material in respect of C, N and O is proportional to the absorption of roentgen radiation at 8—10 Å. The mass absorption coefficient of the reference system has the same wave-length dependence as that of the sample. The results expressed in absolute values are therefore dependent upon the uniformity of the reference system *i. e.*, the mass per unit of area.

Various factors may interfere with the results of the photographic procedure used in the method. A survey is given of such sources of error. The important factor in the photographic and photometric procedure used, the Eberhard effect, is investigated in the primary picture taken at 8—10 Å on the Lippmann film and in the secondary enlargement taken in the visible range on a Kodak 250 plate. Under the photographic conditions used by the authors, the Eberhard effect as a source of error may be excluded.

It is recommended that the intensity of the radiogram should be measured directly with a suitable microphotometer which permits visual control. Such a microphotometer is described.

The procedure reported includes the taking of three microradiograms of fresh, frozen and dried cells, the second and third exposures after extraction by chloroform and enzyme digestion, respectively. This treatment of the section introduces, to a minor degree, fictitious changes in mass due to alterations in the volume of the cell material. This source of error is computed from the surface changes in the section, which are determined planimetrically.

In applying the method to nerve tissue, the lipids are obtained as a difference in weight, expressed in 10^{-9} mg/μ^3, after extraction by chloroform at 20° C. The pentose nucleoproteins (PNP) are obtained in a similar way after digestion by crystalline ribonuclease free from proteolytic effects. Little is as yet known about nucleoproteins and the nature of the linkage between nucleic acid and protein. Digestion by ribonuclease

releases nucleic acids and proteins from the nerve cells; the latter substances are not freed by the enzyme unless nucleic acid is present in the cells. On the basis of this fact and of their microchemical analyses, the authors have — until further knowledge is gained of nucleoproteins — defined the loss in weight occurring during digestion by ribonuclease as the PNP fraction. Pentose nucleic acids appear to constitute about 20 percent of this fraction. The remaining mass represents the residual cell proteins.

In order to compute the errors involved in the extractions, a micro-analysis of nitrogen, phosphorus, carbohydrates and proteins has been performed on frozen sections of the molecular layer of the cerebellum and of spinal ganglia. The conditions were as close as possible to the actual procedure in the roentgen microspectrography.

The method has been applied to analyze Deiters' cells, spinal ganglion cells and Purkinje cells. The results show that the chemical composition of the cells differs quantitatively with respect to lipids, PNP and proteins.

The nerve cells of Deiters' nucleus are characterized by large amounts of lipids and PNP.

The total dry weight of these cells is $1.01 \cdot 10^{-9}$ mg/μ^3, the lipid fraction $0.56 \cdot 10^{-9}$ mg/μ^3 and the PNP fraction $0.25 \cdot 10^{-9}$ mg/μ^3. The differences between these cells and spinal ganglion cells and Purkinje cells are discussed. It is to be noted that all values refer to the volume of the section after the cytologic treatment.

Autoreview.

THE IMPORTANCE OF ADEQUATE STIMULATION FOR THE CHEMICAL COMPOSITION OF RETINAL GANGLION CELLS DURING EARLY POST-NATAL DEVELOPMENT. By Sven-Olof Brattgård. 80 pp, 33 illustrations, 14 tables. Acta radiol. Suppl. 96, Stockholm 1952. Sw. Kr. 20: —.

A report is given of an investigation on the importance of adequate stimulation for the chemical composition of the individual retinal ganglion cells. The most salient data may be summarized as follows.

The experimental material consists of ganglion cells from the ganglion cell layer of the rabbit retina, fixed in Carnoy's solution. The new technique used consists of determinations of the cell mass with soft roentgen radiation, before and after lipid extraction or enzyme digestion of the pentose nucleoproteins (PNP). The method permits determination of the mass of the order of magnitude of 10^{-9}—10^{-10} mg in an area of 4 μ^2. The method is tested experimentally and the results reported. The results are expressed in mass per μ^3 of the cells. The thickness of the cells are determined optically after the cytologic treatment.

The nerve cell exposed to adequate stimulation during the early post-natal period — *i. e.*, from birth to the adult stage — is found to exhibit a considerable increase in the protein fraction. From a mean value of $0.22 \cdot 10^{-9}$ mg/μ^3 at 11 days, it rises to $0.49 \cdot 10^{-9}$ mg/μ^3 at 8 months. The nucleoprotein fraction, which is $0.21 \cdot 10^{-9}$ mg/μ^3 at the age of 11 days, is $0.47 \cdot 10^{-9}$ mg/μ^3 at 10 weeks. No further increase is subsequently found in this fraction.

Variations in the degree of stimulation of the adult nerve cells lead to appreciable variations in the size of the nucleoprotein fraction. An adequately stimulated nerve cell which has a nucleoprotein fraction of $0.49 \cdot 10^{-9}$ mg/μ^3 will have only one-tenth of this size when it is deprived of stimulation for three hours. If the cell is once more stimulated, the size of the nucleoprotein fraction increases. The protein fraction of the nerve cell is unaffected by changes in the degree of stimulation.

The main interest is focused on the relationship of adequate stimulation to the normal development of the chemical components of the nerve cell. The relevant nerve

cells of 10-week-old animals, exposed to adequate stimulation during their whole life, have a protein fraction of $0.31 \cdot 10^{-9}$ mg/μ^3 and a nucleoprotein fraction of $0.47 \cdot 10^{-9}$ mg/μ^3. Corresponding cells from animals of the same age, completely excluded from stimulation from birth onwards, have a protein fraction of only $0.16 \cdot 10^{-9}$ mg/μ^3 and a complete absence of the nucleoprotein fraction. A disturbance occurs in the cellular metabolism of cells from animals born in darkness and living in darkness for the first period of their lives, and is of varying degree in the individual cells. This may be inferred from the results of subsequent stimulation of such cells.

The observations made lead to the following conclusions. The retinal ganglion cells have a high total dry weight as compared to that of other types of nerve cells. In association with the onset of adequate stimulation post-natally, the nerve cells enter a "third growth period". From a point of view of time, the increase in the nucleoprotein fraction precedes that of the protein fraction during the post-natal development of the nerve cells. Adequate stimulation is a prerequisite for the formation of pentose nucleoproteins in the nerve cell. Lack of adequate stimulation during the early post-natal period leads to incomplete development of the nerve cell, and to disturbances in its metabolism and chemical composition.

The observations are presented on the basis of Hydén's theory of nucleoprotein metabolism in nerve cells. Some earlier clinical findings are discussed against the background of the present results.

Autoreview.

GYNÄKOLOGISCHE STRAHLENTHERAPIE. INDIKATIONSSTELLUNG, METHODIK UND ÄRZTLICHE BETREUUNG. Von Richard Kurt Kepp. 232 S. 64 Abb. Georg Thieme Verlag, Stuttgart 1952. DM 26.—.

This voluminous reference book increases the subject, already many metres in length, turned out from the Clinic for Women of the University of Göttingen, by a further two centimetres. It constitutes a special practical part of KEPP's recently published work 'Grundlagen der Strahlentherapie'. The author has included every detail within the gynaecologic orbit of malignant and non-malignant diseases and with German thoroughness has weighed up all the methods generally employed in all the other clinics and radiotherapy centres. He describes the methods of the Göttingen school and points out their high merits. Compared with the easily read Anglo-Saxon literature, the German is perhaps somewhat heavy but should one have reached a certain stage of development in the realms of gynaecologic radiotherapy, the good style of KEPP's book will prove to be of inestimable value.

It is unneccessary to enter deeply into various details and criticisms of methods of treatment. He has diligently quoted the Swedes — HEYMAN, KOTTMEIER, BENNER, INGELMAN-SUNDBERG and NORMAN. Hysterography in cancer of the body of the uterus as well as electronic irradiation in cancer of the vulva are included. The work is exhaustive and will hardly be read right through but rather used as a reference book. As such it is particularly suitable. KEPP follows in the footsteps of his teacher, MARTIUS.

Gunnar Gorton.